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POST-MENOPAUSAL BLEEDING

JAMES T. LOUW, CH.M., F.R.C.O.G.

Professor of Obstetrics and Gynaecology, University of Cape Town, and Cape Provincial Administration

In life it is essential to be clear in thought. In order to attain this happy yet difficult mental state neat definitions are necessary. Once a fixed point is established the course set by the compass of discussion will be clear cut and will be a relatively easy one to follow. Although the word 'menopause' means 'the last period', as opposed to 'the climacteric' which denotes 'a critical period or change' (the latter referring to the whole physical and psychological period of involutionary change), by common usage the two terms, medically speaking, have become synonymous.

Any bleeding after the menopause—no matter whether the periods ceased normally or through artificial measures—is a serious symptom warranting a careful history with diligent clinical examination and special investigations. *Post-menopausal bleeding must always be considered as cancerous in origin until proved otherwise.* This cannot be stressed sufficiently. It may well be wise to make a slight diversion from the topic of discussion and to include another principle, viz. that *excessive or irregular bleeding at the time of the climacteric is abnormal and must always be regarded as abnormal.* Abnormal bleeding must never be considered a normal phenomenon. It demands pathological explanation. As cancer is detected in about 40% of patients complaining of post-menopausal haemorrhage it may, for purposes of clear understanding, be as well to consider the causes of this bleeding. They may fairly readily be classified as follows:

CAUSES OF POST-MENOPAUSAL BLEEDING

1. *Neoplasms*
   - (a) Malignant
     - Uterine
       - i. Cancer, cervix
         - Ectocervical
         - Endocervical
       - ii. Cancer, endometrium
       - iii. Uterine sarcoma
     - Extra-uterine
       - iv. Ovarian (functioning and non-functioning)
       - v. Cancer, vagina
       - vi. Cancer, vulva
       - vii. Spread from cancer, bladder or rectum
       - viii. Sarcoma of the above organs
       - ix. Cancer, Fallopian tube
   - (b) Benign:
     - i. Fibroid
     - ii. Ovarian
     - iii. Benign tumour of vagina or vulva
     - iv. Cervical polypus
2. *Hormonal: Oestrogen*
   - Hyper-
     - i. Therapy
     - ii. Secretory tumour
     - iii. Rejuvenescence of ovaries
   - Hypo-
     - i. Senile vaginitis
     - ii. Senile endometritis
3. *Inflammations*
   - Acute
   - Chronic
4. *Trauma*
   - Prolapse
     - Denudation of exposed cervix and vagina
     - Pressure sloughing due to corrective pessary
   - Rape
   - Accident
5. *Extra-genital* (difficult or impossible for the patient to localize the origin of the bleeding)
   - (a) Urinary tract lesions
     - Caruncles
     - Other causes of haematuria
   - (b) Bowel lesions
     - Causes of fresh bleeding from and through the anus

Cancer of the cervix uteri is responsible for the majority of the deaths occuring in the gynaecological wards of the Groote Schuur Hospital, Cape Town. It is a disease most commonly found in women of ages ranging between 40 and 45, and relatively often in the post-menopausal age. It is easily recognized in most instances, though recognition cannot take place without a vaginal examination, i.e. both palpation and the insertion of a speculum for inspecting the cervix. The effort required is minimal and the reward of recognizing an early cancer is so great that no one may venture to prescribe before the true clinical assessment has been completed. Under no circumstances should an erosion of the post-menopausal cervix be cauterized before an adequate biopsy has been taken and the histological diagnosis of the lesion established.

Even if the appearance of the ectocervical epithelium is normal, a cancer may yet be lurking in the endocervical canal. Further exploration therefore becomes essential. It is also to be emphasized that, if by some misadventure a previous subtotal hysterectomy has been performed, cancer of the cervical stump must always be kept in mind when subsequent bleeding takes place.

Endometrial cancer. The clinical finding of an enlarged uterus for her age in a patient complaining of bleeding after the menopause is significant. However, the size of the uterus is often totally unrelated to the cancer it may harbour. Therefore, all women presenting themselves with this symptom should be subjected to a painstaking, gentle, but thorough diagnostic curettage. Endocervical curettage is an essential part of the operation. The search for cancer should be thoroughly done. X-ray hysterography, at times, is of great assistance, indicating to which region, possibly behind a fibroid, or in pyometria, the curette should be directed.

Good observation has brought to light that a large-framed, relatively infertile, hypertensive woman who gives a story of a meno- and metrorrhagic climacteric period and a late menopause, and who has diabetes, is likely to develop endometrial cancer. It is of interest that of the 134 patients admitted to Groote Schuur Hospital during the period 1952-57, 27 had either frank diabetes or abnormal blood-sugar curves. A further analysis of this finding will be presented shortly.

Bleeding after the menopause may be found in association with large *ovarian tumours*—whether malignant or benign, functioning or non-functioning. Obviously the bleeding found in association with functioning tumours is mainly due to hyper-oestrogenism. The endometrium responds to the hormonal stimulus and with the flow and ebb of the circulating oestrogen it either grows or sloughs. In all probability the uterine bleeding found in association with large genital tumours is due to the various congestions mechanically produced by these lumps.

Sloughing and ulceration of a surface will result in bleeding. It is therefore also found in *cancers of the vulva and vagina*, whether primary or secondary.

Sarcomata of the genitalia are uncommon and may be the cause of bleeding.

As a general rule *fibroids* decrease in size after the involutionary change of the menopause. However, bleeding may be caused if the fibroid increases in bulk owing to a degenerative change or if it becomes submucous and pedunculated. Erosion of the surface of the fibroid tumour may result in profuse bleeding; in rare cases this occurs also with *benign vaginal and vulval lesions*.

Oestrogen excess. As normal endometrial bleeding is dependent upon hormonal influences, and as oestrogens are endometrial 'building' hormones, it does not require any stretch of imagination to realize that if oestrogens are administered for long periods, e.g. for controlling adverse menopausal phenomena, endometrial growth will result. Variation in the amount of circulating oestrogen will affect the endometrium, and may produce sloughing with concomitant bleeding. The same effects will be produced by tumours that produce oestrogen, e.g. granulosa-cell tumours or thecomata. In some women, for an inexplicable reason, a rejuvenescence of the ovaries occurs postmenopausally. This will result in oestrogen secretion, in turn followed by vaginal bleeding. Curettage will reveal endometrium in the proliferative phase.

Oestrogen deficiency, on the other hand, leads to vaginal and endometrial cellular atrophy. Haemorrhagic 'spotting' from these surfaces may therefore occur in the clinical conditions of senile vaginitis and senile endometritis. Of great importance, however, is the fact that with cellular atrophy infection may readily supervene. Both acute and chronic infection may produce a blood-stained vaginal discharge. Should the cervix be occluded, pus will collect in the uterus, which gradually distends and becomes a veritable bag of pus —pyometra—a condition frequently associated with uterine cancer.

Trauma. With the decrease in oestrogens following the menopause, the supports of the genitalia are adversely affected and symptoms and signs of a previous 'weakening' in this region may become aggravated. A prolapse may proceed apace and unless properly attended to will become complete. As the cervix is at the tip of the now inverted vagina, the area around it gradually becomes denuded of epithelium because of constant trauma and a poor return of venous blood and lymph. The ulcer so formed remains indolent until treated by vaginal replacement, hormone administration and cleanliness. An improperly fitting or rough-surfaced pessary will also erode away epithelium and be responsible for the production of an ulcer with bleeding. Vulval and vaginal injury by rape or by accident (falling on a hard object) will obviously cause bleeding.

Extra-genital bleeding. Not infrequently women state that their underclothes are bloodstained but that they cannot locate the origin of the bleeding; it may come from the urethra, vagina or anus. Inspection may reveal a caruncle or a bleeding pile, or the history and physical findings will point to urinary, anal or rectal pathology.

CONCLUSION

Very briefly most of the major causes of post-menopausal bleeding have been discussed. It must always be borne in mind that, no matter whether, for example, senile vaginitis or a urinary caruncle is found, the onus of making sure that a hidden cancer does not exist in the genital tract falls squarely on the shoulders of the medical attendant. It certainly will not benefit the patient if she is treated for senile vaginitis when, in addition, she has a cancer of the endometrium.

No woman who suffers from post-menopausal bleeding should be treated before cancer has been properly excluded. Any deviation from this principle will lead to untold and unnecessary suffering. The treatment for cancer is radical and possibly even maiming. The longer the disease has been missed clinically, the poorer are the patient's chances of survival. How sad it is to know that more mistakes in diagnosis are made by not thinking than by not knowing! Together we must be on guard against this mental trap of sluggish thought and deed.

CONSIDERATIONS ON THE AETIOLOGY OF URINARY CALCULI*

CYRIL WIGGISHOFF, M.A., B.M. (OXON.), F.R.C.S. (ENG.), F.R.C.S. (EDIN.), *Johannesburg*

In 1934 Mr. Swift Joly,[1] Senior Surgeon to St. Peter's Hospital for Stone, London, whose book on Stone is a classic, remarked in his Ramon Guitteras lecture to the American Urological Association that the incidence of urinary stones had greatly diminished in the previous century. This had occurred principally in countries where living standards had improved, and mainly amongst children and young adults. In marshalling factors he considered to be of importance in the aetiology of urinary calculi he brought out the following points.

(A) *Geographical distribution.* Well demarcated areas exist where stones are more commonly found. These areas differ from one another geologically, climatically, and phylogenetically, and no common denominator to account for the higher incidence of urinary calculi in the populations of these localities has been found.

(B) *Diet.* Urinary stones are commoner where cereals are the staple food, and this ties in to a certain extent with the geographical distribution of stones, but by no means explains it completely. For instance, Southern China, which is a stone area, has rice as its staple diet, yet this is generally considered to have a lower

* This paper was presented at the Surgical Club of the University of Illinois, Chicago, 12 June 1958.

stone-forming potential than cereals such as whole-meal flour or oatmeal. At the time of this lecture, vitamin A was in vogue as an aetiological factor in urinary lithiasis; it was believed that the desquamated epithelial cells resulting from a deficiency of vitamin A formed nuclei on which urinary salts were precipitated, but this theory, attractive from a therapeutic point of view, is now largely discredited.

(C) *Disease.* 1. Immobilization leads to decalcification of the skeleton and this may give rise to the formation of renal calculi. This occurred frequently in cases of tuberculosis when immobilization was first instituted as part of the treatment of this disease, and it still occurs in patients who are paralysed by poliomyelitis and other conditions.[2]

2. Urinary stasis is a potent factor in calculus formation; the most frequent examples of this occur in hydronephrosis and in bladder-neck obstructions.

3. Urinary infection is often associated with urinary lithiasis but it is difficult to determine in most instances whether infection is the cause or the effect of the stone.

4. Hyperparathyroidism appears to be a more frequent factor in the incidence of bilateral or recurrent urinary calculi than was at one time recognized,[3-5] but reports on the association of the two conditions vary enormously.

(D) *Metabolic defects.* Certain individuals have increased urinary excretion of uric acid, cystine or xanthine amongst other products of body metabolism. These substances may precipitate to form calculi but their presence in urine does not mean that calculi will necessarily be formed.

In concluding his lecture, Swift Joly stated the theory of the mechanism of stone formation as understood at that time: 'Normal urine is a supersaturated solution of stone-forming salts held in solution by the adsorption action of the urinary colloids. Any condition which reduces the surface area of the colloids reduces the solubility of the stone-forming salts'.

In the past quarter of a century much work has been done to elucidate the causation of urinary calculi and many concepts have been refuted or have had to be modified. Most work has been to discover why stones form, but little has been done to explain how they form. The first major advance in this field was made by Randall,[6] who in 1937, reported the results of his observations on kidneys which he had laboriously and painstakingly dissected at autopsy. He discovered minute calcium plaques in the interstitial tissues of the renal papillae. Small calculi were seen arising from these plaques where they had eroded through the papillary membrane and he believed they form the nuclei on which the urinary salts precipitate. This process was thought to be a degenerative one, and no further advance was made until 1953, when Carr[7] put forward his theory on the formation of renal calculi. He examined kidneys by micro-radiographic techniques both at operation and at autopsy. The kidneys were cut in fine slices and any calculi, no matter how small, were analysed. By this technique nearly all kidneys from patients over 9 years of age were shown to have concretions large enough to be visible to the naked eye. It was demonstrated that in reality the plaque described by Randall is composed of multiple concretions aggregated together. Smaller concretions gravitate to join the larger ones at the tips of the papillae. Behind the base of a large stone smaller ones are found and, behind these, concretions of diminishing size. This explains why some patients continue to pass one stone after another from the same calyx. The kidney contains extensive lymphatic plexuses from which efferent vessels pass through the hilum along the renal vessels to the para-aortic glands. There is a ready communication between the calyces and these lymphatics as evidenced by the pyelolymphatic backflow that occasionally occurs during retrograde pyelography. It would appear that these concretions are normal structures due to the precipitation of salts, and their mechanism of excretion is through the lymphatics in a manner analagous to the removal of foreign particles from the alveoli of the lungs to the mediastinal lymph nodes. Renal calculi may arise when the drainage mechanism breaks down as a result of one of the following factors:

(*a*) Overloading of the excretory mechanism by an excessive number of microliths, as occurs in disorders of calcium metabolism.

(*b*) Impairment of lymphatic drainage caused by fibrosis consequent on inflammatory processes. Concretions become arrested, pressure causes necrosis, and seepage of urine takes place. Once this communication with the collecting system has been established a true renal calculus is born. By diffraction X-ray analysis these concretions have been found to be identical in composition with renal stones.

Urinary calculi are composed of salts and colloids and until fairly recently most attention has been focused on their salt content. With advances in colloid chemistry the urinary colloids are attracting more serious study but much remains to be done in this field. In 1946 Prien[8-10] published the first of his classical papers on the composition of urinary calculi and refuted much that had until then been accepted as fact. Crystalline substances may be analysed by chemical, optical or X-ray methods. Before Prien's work, chemical analysis had been relied on to determine the composition of urinary calculi, and this had given rise to many false presumptions. Prien employed methods which are not only more accurate in analysing crystalline materials, but which may also be employed in the analysis of minute quantities of ground material taken from different portions of the stone. Over 6,000 urinary calculi were eventually analysed by these methods and were divided into the following groups:

(*a*) 67% were pure calcium oxalate or mixtures of calcium oxalate and apatite. These are the 'hemp seed' stones which usually arise in acid sterile urine.

(*b*) 21% were phosphatic calculi, which include pure stones of triple phosphate and mixed stones composed of triple phosphate and apatite. These 'staghorn' calculi occur most often in alkaline infected urine.

(*c*) 6% were uric-acid calculi.

(*d*) 4% were cystine calculi.

(*e*) 2% were xanthine and indigo calculi.

Apatite is a complex calcium phosphate, sometimes containing carbonate. Calcium carbonate as such is not found in urinary calculi. By these studies, the theory that calculi developed on a nucleus of pus, desquamated cells or bacteria was shown to be highly improbable and it has lost ground ever since.

The hypothesis has been advanced that urine is a supersaturated solution of salts which precipitate at varying pH, thereby forming centres of crystallization which act as nuclei for the further deposition of urinary salts. The composition of urinary stones would then depend on the degree of supersaturation of the various salts and the pH of the urine at any time. With increasing alkalinity the solubility of apatite and triple phosphate diminishes markedly, while the solubility of calcium oxalate remains fairly constant. Infection influences stone formation largely through its effect on urinary pH. As was demonstrated by Prien, only about 21% of calculi are associated originally with infection. These are staghorn calculi of triple phosphates, either pure or mixed with apatite. It should be noted, however, that not all staghorn calculi are associated with infection. Pure apatite stones are not common, but when they occur, they are frequently staghorn and the urine is acid and uninfected. Analysis of a series of triple phosphate stones has shown them to be associated most frequently with the following organisms:[11] Micrococcus 38%, *B. proteus* 24%, *E. coli* 12%, Pseudomonas 12%, Aerobacter 5%, Staphylococcus 5%, Streptococcus 4%. These are the so-called 'urea-splitting' organisms, which produce ammonia and thereby render the urine alkaline. The influence of the urinary pH on stone formation has formed the basis of the treatment of urinary lithiasis in which the pH of urine is altered by various drugs. The dilution of the urinary salts by a high urinary output consequent on high fluid intake has also been advocated for many years. Unfortunately, as a result of improved methods of chemical study, serious doubt has been cast whether, in fact, the stone-forming salts in urine are in a supersaturated state.[12]

As already noted, the importance of urinary colloids has been assumed for a long time, but not until recently have suitable methods for their study been devised. Colloids, or materials in a state of colloidal suspension, are in a position between the microscopic and molecular systems. They appear to be clear to the naked eye or when viewed under the ordinary microscope. When examined under the ultra-microscope they exhibit Brownian movement. It has been estimated that 1 g. of colloidal material in urine has a surface area of approximately 5,000 square metres. One of the most important consequences of this is the unsaturation of the ions located on the surfaces of the colloidal particles, causing adsorption of ions dispersed in the surrounding medium. This is accompanied by the formation of electrical charges around

the particles, preventing their coalescence into larger aggregates. Furthermore, sedimentation of finely divided particles may be almost completely counteracted by the Brownian motion of the colloid. Certain electrolytes are effective in the precipitation of some colloids and, as concentration of urine relatively increases the proportion of electrolytes and decreases the proportion of colloids, the possibility of their precipitation is thereby greater. This may explain dehydration as a factor in stone formation.

In 1951 Butt[13] published his paper on the role of the protective urinary colloids. It is a well-known fact that urinary calculi are extremely uncommon in the Negro races irrespective of their social, economic or domiciliary status. Butt found that the colloidal activity in the urine of Negroes was much higher than in Whites. In fact the only urine from a Negro which showed low colloidal activity was from one who was found to be harbouring a renal calculus. Urine from White patients with urinary calculi displayed significantly lower colloidal activity than in the control group without stones.

As more and more work is done on this important problem, so the issues become more complex. What 25 years ago could apparently be explained by a relative simple theory has been replaced by a number of complicated physical and chemical phenomena which are difficult to correllate; and still we seem no nearer a solution to the problem. This is reflected by the fact that in a quarter of a century no real advance has been made in the prophylactic treatment of urinary calculi.

SUMMARY

The literature of the past quarter of a century on the aetiology of urinary calculi is reviewed. Although the concepts regarding the formation of urinary stones have had to be modified as a result of the advances in chemical and radiological methods of investigation, no real advance in the prophylaxis of urinary lithiasis has resulted.

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ORAL HYPOGLYCAEMIC AGENTS IN DIABETES MELLITUS*

CHLORPROPAMIDE AND OTHER HYPOGLYCAEMIC AGENTS IN DIABETES, WITH SPECIAL REFERENCE TO CHLORPROPAMIDE IN SECONDARY TOLBUTAMIDE FAILURE

J. B. HERMAN, B.Sc., M.B., CH.B., *Department of Medicine, University of Cape Town*

The comparative action of various hypoglycaemic agents used in diabetic patients was studied.

Glucose-tolerance tests and fasting blood-sugar estimations were charted in a number of patients over a period of years. This long-term study, in which each patient acted as his own control, yielded interesting information about the natural course of diabetes, showing remissions and relapses in the disease. The sulphonylureas, carbutamide (BZ 55), tolbutamide (D 860, Rastinon, Artosin) and chlorpropamide (Diabinese) were used successively in the same patients.

Carbutamide was shown to be a very effective hypoglycaemic agent—some cases showing a normal glucose-tolerance test in addition to normal fasting blood-sugar levels.

Tolbutamide was not quite as effective as carbutamide. Secondary tolbutamide failure and the subsequent response to the latest sulphonylurea, chlorpropamide, were demonstrated.

In 26 diabetics, in whom the disease started in maturity and who were treated with chlorpropamide, 23 showed a good or moderate response, and 3 no response. None of a further 4 acute-onset (juvenile type) diabetics showed any response to a trial with Diabinese.

Chlorpropamide was thus found to be a powerful hypoglycaemic agent in diabetes of late onset and also in secondary tolbutamide failure.

* Abstract of paper presented at Research Forum, University of Cape Town, 1 September 1959.

FORTHCOMING INTERNATIONAL MEDICAL CONFERENCES

The First International Congress on Medical Photography and Cinematography will be held in Cologne, Germany, on 27-30 September 1960, in connection with the 'photokina' on 24 September–2 October at Cologne. The purpose of the Congress will be to show the present status of photographic and cinematographic exposure and reproduction technique in medicine. The Congress has been organized by the *Deutsche Gesellschaft für Photographie e.V.*, Neumarkt 49, Köln, Germany, who will supply detailed information on request. The programme will not be available until May 1960. The closing date for registration of lectures will be 15 March 1960 and the closing date for registration of personal participation will be 1 August 1960. The registration fee will be DM 30.00 until 1 August 1960, but after that it will be DM 40.00. A day ticket will be DM 10.00.

The Seventh International Conference of the International Society of Geographical Pathology will be held in London on 28-30 June 1960. The subject of the Conference is 'Eclampsia and pre-eclampsia in pregnancy'. Members who wish to contribute to the scientific proceedings are requested to submit titles and typewritten abstracts of their papers to the Secretary General, Prof. Fred. C. Roulet, Schaublin-strasse 17, Basel 24, Switzerland, not later than 29 February 1960. Further particulars may be obtained from the Secretary General or from Prof. B. J. P. Becker, Department of Pathology and Microbiology, University of the Witwatersrand, Johannesburg.

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South African Medical Journal : Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL : VAN DIE REDAKSIE

MAGNESIUM METABOLISM

The past decade has brought into prominence the part played by electrolytes in health and disease. So far the main emphasis has been on sodium, chloride, and potassium, and advances in knowledge have been such that clinicians have been able to detect the clinical counterparts of disturbed electrolyte metabolism, readily confirm them biochemically, and institute rational therapy. It is clear that in this field the next step forward will be the elucidation of the part played by magnesium.

Many methods have been developed to estimate the presence of this ion, and most of these are tedious, inadequate and unsuitable for routine use. An instrument is now available which is accurate, relatively simple to use, and able to determine the magnesium content of serum, urine and tissues. The more widespread use of this instrument will greatly increase our knowledge of the role of magnesium in man.

A great deal is already known: The total amount of magnesium in the adult human is about 25 g. One half of this is stored in bone and high concentrations are also found in the liver and striated muscle, the ion being found mainly within the cells. The average daily intake of magnesium in the diet is 250-300 mg. and some of this is unabsorbed and excreted in the faeces, while 60-120 mg. are excreted daily in the urine. There is no known endocrine control of this excretion, but there is evidence that there may be tubular secretion of magnesium as well as filtration by the glomeruli and reabsorption by the tubules.

The normal level of the serum magnesium will vary with the method of estimation used, and each laboratory must establish its own normal levels. These usually lie between 1·5 and 2·0 m.Eq. per litre. It is not known why the level in the cerebrospinal fluid is higher than that in the serum. Part of the serum magnesium is bound to protein (probably about thirty-five per cent). Hypermagnesaemia occurs in renal disease. This may result from the administration of magnesium sulphate to patients with severe chronic renal failure. Hypermagnesaemia may also occur in acute oliguric renal failure, and it is possible that some of the manifestations of depression of the central nervous system in uraemia may be due to an elevated serum magnesium. Magnesium salts should not be given to patients with severe renal disease. However, a low serum magnesium may also occur in renal disease. Hypomagnesaemia has been observed in the recovery phase of acute oliguric renal failure (acute tubular necrosis) and occurs occasionally in pyelonephritis.

Fifty per cent of patients with primary hyperaldosteronism have a low serum magnesium. This state of affairs may also be found post-operatively in patients who receive prolonged parenteral feeding and it tends to occur much more readily in children than in adults. Prolonged diarrhoea in a child may deplete the body stores of magnesium. A percentage of patients after parathyroidectomy are found to be in negative magnesium balance, possibly because magnesium accompanies calcium when it is rapidly deposited in bone. However, some patients are in negative balance even before the parathyroids are removed. A lowered serum magnesium may be associated with tetany, neuromuscular irritability, and confusion, and this may be corrected by the administration of magnesium. Most workers have failed to confirm that magnesium deficiency plays any part in epilepsy or alcoholism, and the low serum magnesium sometimes found in acute pancreatitis or diabetic acidosis has no known important accompanying symptoms or signs. There are no known electrocardiographic changes due to magnesium deficiency in man.

The next few years should yield the answers to many of the unknown facts about magnesium metabolism.

DIE HIPERVENTILASIE-SINDROOM

Die hiperventilasie-sindroom, of respiratoriese alkalose, is 'n algemene toestand. Die insidensie van die toestand in algemene hospitale en in die praktyk van interniste word beraam op 5-10 persent.[1,2] Nagenoeg 75 persent van die pasiënte is volwassenes van oor die dertig jaar, en vrouens is meer daaraan onderhewig as mans in die verhouding van 3 : 2.[1]

Die simptomatologie van die toestand berus op die feit dat hiperpnee 'n oormaat kooldioksied deur die longe laat verlore gaan vanweë oormatige alveolêre ventilasie. Dit lei tot 'n daling in die kooldioksiedtensie (pCO_2) van die plasma en gevolglik 'n verandering in die elektroliet- en pH-waardes met 'n versteuring in die verskillende metaboliese funksies van die organisme.

Die simptome wissel soms baie, maar afgesien van 'n opvallende hiperventilasie, kla die pasiënte aanvanklik van duiseligheid, mislikheid, en floute. Daar is 'n dofheid en domheid van die vingerpunte met 'n styfheid en prikkelende gevoel om die lippe. Hierop volg 'n gevoel van beklemming in die borskas en sametrekkings van die spiere, hartkloppings, gesuis, en dofheid van gesig. Die vel mag koud en klam wees en sianose mag sigbaar word. Omdat die daling in die pCO_2 van die bloed 'n belangrike prikkel van die asemhalingsentrum verwyder, volg hipokapnie spoedig.

Die beeld mag baie lyk op dié van 'n skoktoestand, veral die stygende polsspoed, dalende bloeddruk en die koue, klam sianotiese vel. Vir die klinikus word die beeld verder gekompliseer deurdat die elektrokardiogram omkering van T-golwe of afdrukking van ST-segmente met afplatting van die T-golf mag toon. Die Q-T-tyd mag verleng wees. Al hierdie veranderings is omkeerbaar deur inaseming van 'n 5 persent CO_2-mengsel.[1]

Pasiënte wat aan hierdie toestand ly is dikwels gespanne mense en hulle het soms 'n verborge vrees vir siekte of die dood. Deur aan hulle te toon dat die simptome na willekeur te voorskyn geroep kan word deur doelbewus te hiperventileer, kan hulle dikwels, indien nie genees nie, baie beter word.[3]

Dit is egter belangrik om te onthou dat hiperventilasie nie *noodwendig* op hierdie basis verklaar moet word nie. Aronson[4] byvoorbeeld, beskryf agt gevalle waar die hiperventilasie-sindroom te voorskyn geroep is deur organiese letsels soos miokardiale infarksie, hiatusbreuk, spontane pneumotoraks, en akute cholesistitis. Waar die sindroom dus in die meeste gevalle 'n psigogene patogenese het, moet 'n mens tog versigtig wees om nie die paar gevalle waar ernstige organiese letsels die verantwoordelike faktore is, sonder meer as psigogene hiperventilasie te bestempel nie.

As daar 'n organiese letsel teenwoordig is, sal dit heelwaarskynlik intratorakaal geleë wees, *of* nèt onder die diafragma, en 'n röntgenologiese en elektrokardiografiese ondersoek mag dus van groot waarde wees.

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TAALRUBRIEK

Die Taalkomitee van die Geneeskundige Skool van die Universiteit van Stellenbosch stel voor om te gebruik:

1. Eng. (an)irritant: Afr. *irritans*, mv. *irritanse*. Die Komitee voel nie baie gelukkig hieroor nie en sou verkies om 'n algemene oplossing te vind vir alle soortgelyke gevalle, bv. ingestant, inhalant, vescicant, e.s.m. Vind ons later miskien iets, sal dit hier gepubliseer word.

2. Eng. malpresentation. Afr. *wanligging*.

3. Eng. laxity: Afr. *slapheid*.

4. Eng. modality: Afr. *modaliteit*.

5. Eng. adherent: Afr. *klewende* of *verkleefde* (b.nw.), bv. 'n klewende of verkleefde plasenta. 'n Algemene woord (s.nw.) sou dan wees 'n verklewing, en i.v.m. pleisters het hegpleister al algemeen geword in die gewone spreektaal.

6. Eng. powers (of labour): Afr. *krag* of *kragte*, en dus bv. baarkrag/barenskrag(te), ens.

7. Eng. ascites: Afr. *askites*. Die Komitee het oorweeg of dit askites of assites moet (of kan) wees, gedagtig ook aan bv. sis (en nie kis nie), ensefalogram (en nie enkefalogram nie), ens. Nou is dit nie so dat die k-vorme ‚verkeerd' sou wees nie, want dan sou askites ook verkeerd wees. Net so min is die s-vorme verkeerd, want dan sou bv. siklus ook ‚verkeerd' wees (Grieks is immers *k*uklos).

Nee, die posisie is so: baie van ons woorde kom van Grieks, dikwels *via* Latyn. Grieks het nie 'n c nie, net 'n k, en Latyn geen k nie, net c (en in sommige verbindinge q). In Latyn is daardie c dan in sommige woorde soms uitgespreek as s, veral in Wes-Europese tale wat sulke woorde ontleen het. So kry ons dan soms k- en s-vorme naas mekaar, bv. Caesar (Sesar) en keiser, seramiek en keramiek, ens. Soms het een Griekse k tot 'n s geword, maar in dieselfde woord het 'n ander k behoue gebly, bv. en*sik*lopedie en *sik*lus, wat altwee twee k's het in Grieks, wat niemand tog seker bereid sal wees om uit te spreek en dus te spel en*k*iklopedie en *k*iklus nie, behalwe miskien 'n puristiese Gre*k*is, maar nie Gre*s*is nie. Wat moet ons ander taalmense nou doen? Die Taalkomitee stel hom op die volgende standpunt; hy aanvaar k- en s-vorme altwee as ‚korrek', maar in sy keuse laat hy hom lei deur wat sprekers sê. As daar getuienis is dat die meeste sprekers k-sprekers is, kies ons die k-vorm (soos in askese), en as die meeste s-sprekers is, dan die s-vorm (soos in sis). Het ons nie voldoende getuienis dat k- of s-vorm oorheers nie, bly ons by die letter van die geval, soos in askites.

8. Eng. cirrhosis: Afr. *sirrose*.

9. Eng. brittle: Afr., van bene gebruik: *bros*, dus bv. bros bene, maar van bv. diabetes gebruik: *moeilik beheerbare*, en daarby dan die juveniele en die labiele tipes.

10. Eng. borborygmi: Afr. *dermklanke*.

11. Eng. cervical: Afr. *servikaal*, *servikale*, en s.nw. *servisitis*. Daar is geen beswaar teen die gebruik van hals- en nek- waar hulle pas nie, bv. nekwerwels, halswerwels.

Dit kan mense as vreemd tref dat ons servi*k*aal met 'n *k* aanbeveel, maar servisitis met 'n *s*. Ons wys dan net daarop dat so 'n wisseling baie gewoon is in Afr., sy dit dan in 'n ander tipe woord, bv. fabrie*k*: fabriseer; polemiek: polemiseer; kritiek: kritiseer, ens. En verder kan ons dink aan bv. appendi*k*s: appendisitis; larin*k*s: laring*i*tis.

12. Eng. base: Afr. *basis* (bv. van die long en die skedel), mv. *basisse*.

13. Eng. caries: Afr. s.nw. *kariës* (uit Latyn) en b.nw.: *karieus*.

14. Eng. bio-assay: Afr. *bio-essai*.

15. Eng. micturate: Afr. *miktureer*, en micturition: *miksie*. Mikturisie kan later oorweeg word indien daar 'n betekenisonderskeiding sou ontstaan.

16. Eng. urinate: Afr. *urineer*.

OBSERVATIONS ON THE USE OF THE ARTIFICIAL KIDNEY*

J. G. FOSTER, M.B., B.CH. (RAND), M.R.C.P. (EDIN.), *Physician to the Ernest Oppenheimer Hospital, Welkom*

The Ernest Oppenheimer Hospital provides full medical services for a labour force of about 38,000 Natives. In spite of safety precautions underground mining for gold is still a hazardous occupation. In our experience over the past 7 years, many severely traumatized patients, especially burned cases and those who incurred prolonged periods of hypotension, may develop a more or less complete renal shut-down. This is anticipated and treated by adjustment of the fluid balance and serum electrolytes, but the outcome is nevertheless sometimes fatal. It was therefore decided to acquire a Kolff-type of 'artificial kidney', the use of which might tide the patient over reversible kidney lesions.

This Travenol 'disposable twin-coil kidney'[1,2] has been used so far on 3 occasions in this hospital. It is intended to

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describe its use in our metabolic unit, some practical points, and some difficulties that have arisen.

The Principle of the Coil Kidney

The coil kidney consists of two lengths of cellulose tubing enveloped in fibre glass screens which are wrapped around a central cylinder. This tubing acts as a semi-permeable membrane. The heparinized blood is pumped through it at the rate of 200-400 c.c. per minute.

Dialysing fluid, the composition of which can be altered to suit each case, circulates around these tubes, and by processes of osmosis, hydrostatic pressure and simple filtration the blood is brought into equilibrium with the surrounding dialysing fluid. When this stage is reached further dialysis of the blood can be obtained only by renewing the dialysing fluid. The composition of this fluid, which is almost standardized, is as follows:

mEq. per litre		*g. per* 100 *litres*	
Sodium	133	NaCl	570
Potassium	5	$NaHCO_3$	300
Calcium	5	KCl	40
Magnesium	3	$CaCl_2$	28
Chloride	110	$MgCl_2$	15
Bicarbonate	36	invert sugar	0·4%

A built-in thermostat maintains the dialysing fluid at a constant temperature (39°C), and the pH of the fluid must be kept at approximately 7·4 in order that no haemolysis of the blood shall occur.

The average urea clearance obtained during dialysis is from 100 to 300 c.c. per minute,[3] depending on the rate of flow through the coils.

Team-work in the use of the artificial kidney is of the greatest importance, for the procedure occupies several hours. In the early stages good team-work enables the preparation of the patient and the priming of the 'kidney' to be completed simultaneously.

Routine pre-operative skin preparation of the arms and legs from the knees to the umbilicus is performed by the nursing staff in the general ward. The patient is then transferred to the metabolic ward, where the selected blood-vessels are exposed by the surgeon.

The priming of the 'kidney' is under the control of the physician and an assistant; it entails the assembly and testing of the apparatus, the preparation of the required dialysing fluid, and the filling of the inflow tubes, the coil and the outflow tubes with 2-3 units of inter-matched heparinized blood. Each unit must also be individually cross-matched with the patient's blood.

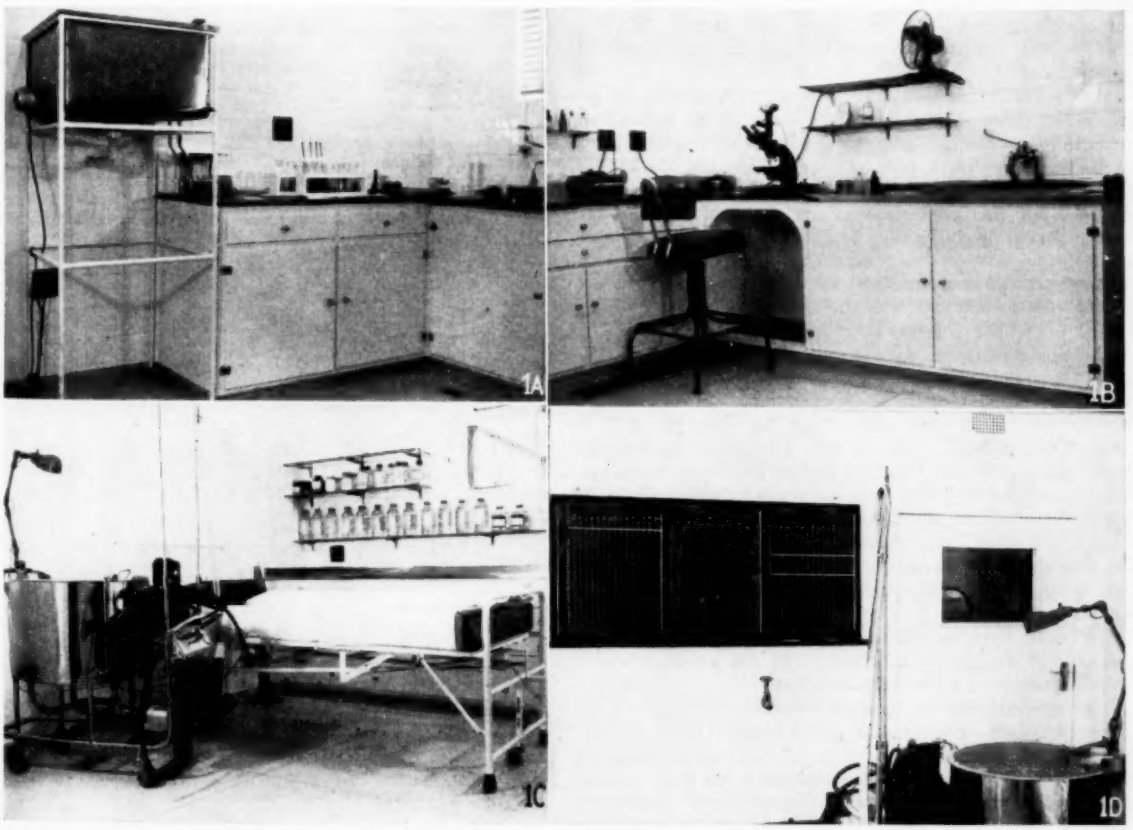

Fig. 1. A and B are views of the preparation room showing separate tank for preparation of new dialysing solutions, etc. C and D are views of the dialysis room showing the 'artificial kidney' etc. Beneath the blackboard is the tap which allows fresh dialysing solution to be run from the tank shown in A into the 'kidney' when change-over of the solution is necessary.

At this stage the patient is heparinized, the cannulae are inserted into the exposed vessels, which are then attached to the input and output tubes on the 'kidney', and the machine is switched on. It should be possible to accomplish this 30-45 minutes after beginning the preparation.

There is constant supervision of the patient by a nursing sister throughout the haemodialysis. She records the pulse rate and the blood pressure every 5 minutes, and informs the house-surgeon of any change. This is particularly important during the first 30 minutes after the operation commences.

The house-surgeon watches the apparatus for any dangerous rise in pressure in the coil and any leak that may occur through it. If either happens the machine is switched off until the fault is corrected. Samples of blood are taken from the circuit half-hourly for estimation of the serum electrolytes and blood urea, and to check on the clotting time. These investigations are carried out by the technician in the clinical laboratory, and the results are charted. The pH of the dialysing solution is checked hourly by the laboratory technician and is adjusted by altering the rate of flow of carbogen through the solution.

In this hospital a metabolic ward is set aside for artificial-kidney procedures. It consists of two adjoining rooms each about 13 × 12 feet in size (Fig. 1). Their floors, made of terrazzo, are sloped to drain any spill of old dialysing solution that may occur during replacement with the fresh solution.

One room is the 'preparation room', which is used for the initial priming of the machine and for the subsequent preparation of fresh dialysing solutions during haemodialysis. It is therefore fitted with cupboards for the storage of chemicals, intravenous solutions and drugs that may be required for the 'priming' and during haemodialysis. A spare 'disposable coil' must always be available as a replacement in the event of a fault occurring in the one being used. The preparation room is also used during haemodialysis for the half-hourly estimation of the serum electrolytes and the hourly pH of the dialysing solution.

Haemodialysis takes place in the second or 'dialysis room', when the vessels have been exposed and the primed artificial kidney has been wheeled through. It is equipped with a Fowler bed fitted with soft dunlopillo mattress, and a surgeon's hand-basin. Blackboards are fixed to the wall to chart graphically the levels of the serum electrolytes and blood urea and the blood pressure of the patient.

Carbogen, oxygen and nitrous oxide are piped through to the dialysis room. Carbogen is constantly bubbled through the dialysing solution to assist the maintenance of the pH, and oxygen and nitrous oxide are immediately available should they be required.

An operating-table type of anaesthetic screen is fitted to the side of the patient's bed, so that the actual artificial kidney is obscured from the patient's view.

The efficiency of the dialysis depends on the relative electrolytic and metabolic differences between the dialysing fluid and the patient's serum and after dialysis has continued for 1½ - 2 hours it is usually advisable to renew the dialysing solution according to the patient's requirements. To hasten this change-over a separate tank (also thermostatically controlled at a temperature of 39°C) is provided, so that the new solution can be prepared immediately before the change-over is effected. By this means 'lost' dialysing time is reduced to a maximum of 10 minutes, which is the time required to drain and refill the tank.

CASE REPORTS

Case 1

The first case treated with the artificial kidney was one of chronic renal insufficiency. The indications for dialysis in chronic renal insufficiency are not well defined. Merrill[4] suggests 3 indications, viz. (1) when intercurrent stress overtaxes the renal reserve, (2) to relieve the nausea, vomiting and anorexia of patients whose course has been gradually downhill, (3) to prepare patients with chronic nephritis and renal failure for necessary operation, or when renal decompensation has occurred after surgery. This patient was a case of uraemia, thought to have been precipitated by an intercurrent pulmonary infection, in a young tropical Native with previously compensated chronic renal disease. A severe normochromic anaemia attributable to the renal condition was also present.

The immediate treatment given included the use of (*a*) antibiotics to combat infection, (*b*) the restriction of fluid intake (protein-free) with adequate calories in the form of glucose, and (*c*) blood transfusion. The initial response was good, with improvement in the urinary output, and the infection appeared to be under control. However, about 2 weeks later, while he was still on restricted fluids, deterioration commenced. Oliguria developed and a pericardial friction rub and a protodiastolic gallop were heard. There was a slight diarrhoea and the patient gradually began to show signs of mental involvement. On 4 June 1959 he was mentally clouded and drowsy, and in addition the serum potassium had risen to 9·12 mEq. per litre.

As it was still hoped that compensated renal function would return to the extent that the patient could be sent home, it was decided to apply haemodialysis immediately. However, 3 hours elapsed before the dialysis began, owing firstly to the time necessary for the 4 units of blood to be crossed and inter-matched, and secondly to precipitation occurring in the dialysing solutions when the calcium and magnesium chloride were added. It became evident that the pH of the solution must be brought to 7·4 *before* the calcium and magnesium chloride are added.

Thirty minutes after dialysis began, back-pressure on the output side of the coil developed owing to an obstruction in the 'venous'

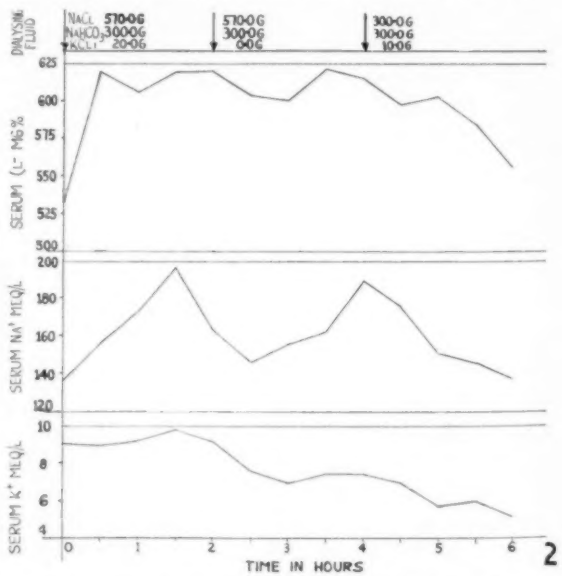

Fig. 2. Graph showing the biochemical results during haemodialysis in case 1. The arrows indicate the time of renewal of the dialysing solutions and the weights of NaCl, $NaHCO_3$ and KCl per 100 litres used in each solution are shown.

cannula. This necessitated replacement of the polythene cannula and change in the cutdown. In spite of this the pressure again built up, and remained high throughout the procedure. The use of a Martin's blood pump on the output tubing reduced the back-pressure sufficiently to prevent a dangerous rise in pressure in the coil. Haemodialysis continued for 6 hours, and the results of the serum electrolytes are shown in Fig. 2.

By the end of dialysis there was an obvious improvement in the patient's condition—he was no longer drowsy, and the proto-diastolic gallop had disappeared. There was, however, no improvement in the renal function and the patient's condition became worse about 4 days later. Death from uraemia occurred on the 8th day after dialysis.

Post-mortem examination showed small contracted kidneys with granular surfaces and reduced cortico-medullary ratio. The heart was enlarged, and there was a moderate straw-coloured pericardial effusion. Terminal broncho-pneumonia was present. Histological examination confirmed the diagnosis of chronic glomerulonephritis.

Case 2

A Shangaan male, aged 25, was admitted to hospital on 1 September 1958 with severe second-degree burns after an explosion of methane gas underground; 60% of the body surface was involved.

Routine treatment was instituted and for the first 2 days the urinary output was satisfactory, with good concentration. On the 3rd day his general condition had deteriorated, and although the urinary output was still good, the specific gravity varied between 1,012 and 1,014. There had been a slow rise in serum potassium with a falling blood pressure. On the 4th day the serum potassium was 7·25 mEq. per litre, and in spite of a good urinary output it was decided to perform haemodialysis.

Dyspnoea and cyanosis came on suddenly 2½ hours after dialysis was begun, and the blood pressure dropped. In spite of resuscitative measures the patient died, and at autopsy a massive pulmonary infarction was found, due to embolism from deep-vein thrombosis in the calf. The effects of haemodialysis in this case are shown in Fig. 3. During the procedure it was again noticed that there was a moderate rise in back-pressure on the output side of the coil, but no active measures to counteract this were necessary.

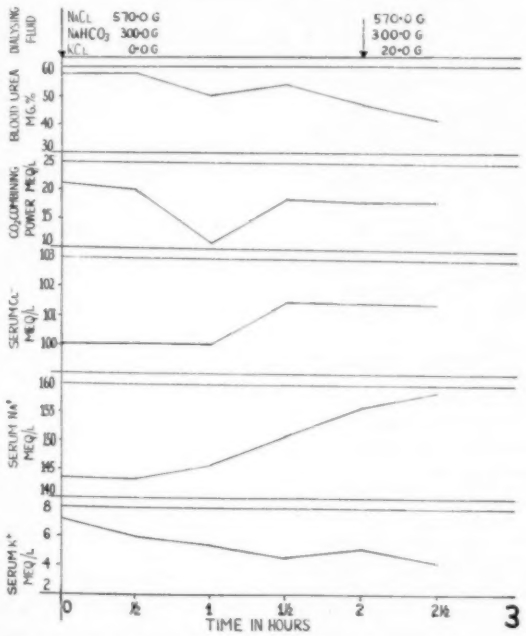

Fig. 3. Graph showing the biochemical results during haemodialysis in case 2.

Case 3

A 29-year-old Native from the Northern Transvaal, suffering from tuberculous osteitis of the spine, underwent a spinal fusion on 24 October 1958. The operation was uneventful, 2 units of blood being given as routine. A few hours after the operation he became restless, and there was severe bleeding from the operation wound. He was severely shocked, and for 6 hours the systolic blood pressure fluctuated between 80 and 90 mm. Hg.

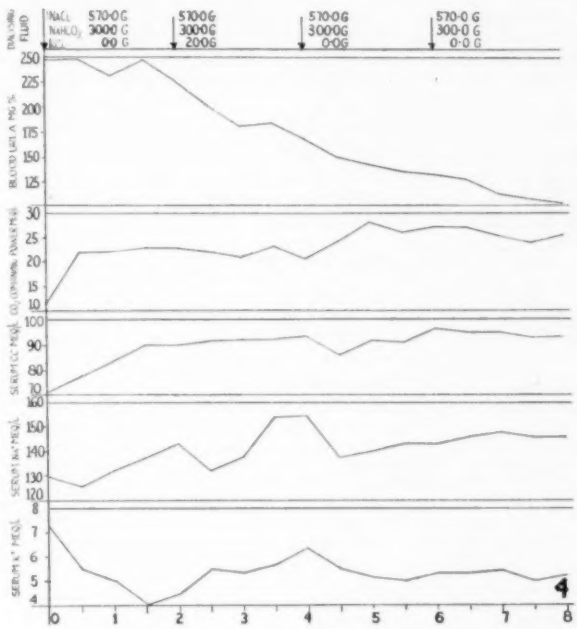

Fig. 4. Graph showing the biochemical results during haemodialysis in case 3.

It was subsequently proved that a major blood-transfusion incompatibility had occurred. The patient was Group O Rh-positive, and owing to an error in interpretation of the cross-match he had received 500 c.c. of blood from a Group-A Rh-positive donor. A coagulation defect occurred as a result of the transfusion reaction, and oozing continued for 12 hours.[6]

Treatment consisted of transfusion of further carefully cross-matched blood, with intravenous cortisone and noradrenaline to maintain the blood pressure, and subsequently restriction of the fluid intake. For the first 4 days there was complete anuria. On the 5th day the patient passed 200 c.c. of dark urine but his general condition was worse. The serum potassium was 5·5 mEq. per litre and the blood urea 250 mg.%. On the 7th day he was severely acidotic (CO_2 combining power 12·0 mEq. per litre), the blood urea was 320 mg.%, and the serum potassium was 7·0 mEq. per litre, with early ECG changes of hyperpotassaemia. The urinary output had fallen to 60 c.c.

Haemodialysis was performed and continued for 8 hours. Although electrolytic improvement was noted during the procedure (Fig. 4), clinical improvement was not apparent until 6 hours later. (Note: No back pressure on the coil developed during haemodialysis in this case. This was attributed to the larger polythene cannulae used, and to the fact that they were carefully rinsed with heparin before use.)

Subsequently the patient made good progress. The urinary output increased daily, and by the 16th day after dialysis he was passing 2,000 c.c. of dilute urine daily. Unfortunately he died suddenly on the 21st day as the result of a large pulmonary embolus lodged at the bifurcation of the pulmonary artery.

At post-mortem the kidneys were slightly pale in appearance but were otherwise normal.

DISCUSSION

Notwithstanding the fatal outcome in these first 3 cases, their favourable response to haemodialysis confirms the usefulness of the artificial kidney as part of the management of renal insufficiency.

The operation of the Kolff 'disposable coil' type of artificial kidney is not difficult,[6] but it must be stressed that an experienced team of operators with a well-equipped metabolic unit is essential for the efficiency of the whole procedure with the minimum of danger to the patient. It is also considered important to record the electrolyte and urea levels and the CO_2 combining power half-hourly. This not only ensures that effective dialysis is taking place and that the machine is operating properly, but also enables one to gauge better when to renew the dialysing fluid and to adjust its composition. A few other points have merged during our experience with the 'kidney'.

Choice of Blood Vessels for Cannulization

In all 3 cases the most effective combination of vessels used was that of the radial artery and the inferior vena cava. A blood flow of at least 200 c.c. per minute is available through the radial artery,[3] and at this rate the urea clearance is approximately 140 c.c. per minute. The inferior vena cava, cannulated *via* the saphenous vein, is used on the output side. It has been our experience that back-pressure may develop at this place, but this danger is minimized by using well-heparinized large-bore cannulae (size 3-5 mm. internal diameter).

For cases that may require repeated dialyses it is suggested that the Seldinger technique[7] can be used on the femoral artery at the input side in cases where both radial arteries have already been used.

Heparinization of the Patient

8,000 – 10,000 units of heparin has been recommended for patients of approximately 75 kg. weight. It is our experience that this dosage increases the coagulation time to more than 60 minutes, and it would seem that 5,000 units is sufficient for the average patient. In cases 1 and 3 a further 2,000 units was required halfway through the procedure to maintain an adequate coagulation time.

pH of the Dialysing Solution

Once haemodialysis was started it was noticed in all cases that the solution rapidly became more alkaline and that in order to maintain the pH at a reasonably constant level, it was necessary to bubble the carbogen through the solution very rapidly. Carbogen consists of 10% carbon dioxide and 90% oxygen, and it may well prove better to use 20% carbon dioxide and 80% oxygen.

Citrate Intoxication[8]

Citrated blood which is also heparinized (2,000 units to each unit of blood) was used for the 'priming' of the kidney. In cases 1 and 3 citrate intoxication tended to occur during haemodialysis, in spite of the intravenous administration of 10 c.c. of 10% calcium gluconate for every unit of blood used. As soon as any fall in blood pressure was noticed a further 10 c.c. of calcium gluconate was given, and this dramatically restored the blood pressure to normal (Fig. 5). It is therefore suggested that on the occurrence of hypotensive episodes, besides ensuring the proper functioning of the machine, further calcium should be given before other resuscitative measures are applied.

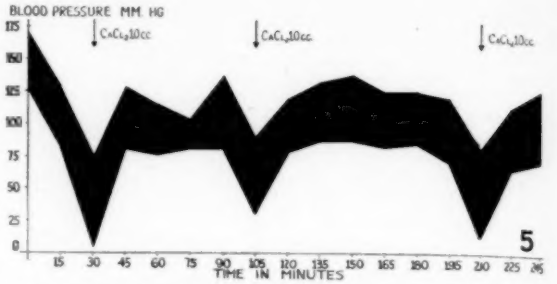

Fig. 5. The blood-pressure chart in case 3, showing the response to intravenous calcium chloride in hypotension due to citrate intoxication.

Time of Dialysis

Although the duration of haemodialysis should be sufficient for elimination of most of the toxic metabolites and renal toxins, and for correction of the electrolytes, it is nevertheless desirable that the time should be as short as possible, because the procedure is extremely exhausting to the patient. For this reason the use of a separate tank is recommended, in which the new dialysing fluid can be prepared shortly before the change-over. It has been found that the time necessary for 8 hours of haemodialysis is thereby reduced by at least 1 hour.

Pulmonary Embolism

Although in cases 2 and 3 the cause of death was pulmonary embolism, the emboli cannot be attributed to the use of the artificial kidney. In case 2, not only was the time of haemodialysis too short for the dialysis to be implicated, but there was post-mortem evidence of pre-existing deep-vein thrombosis in the leg. In case 3 the embolus had originated from a large thrombus in the right iliac vein; this thrombus is thought to have occurred as the result of the preceding 50%-dextrose infusions which had been given through a polythene cannula in this region.

During the oliguric phase it is necessary to maintain a certain intake of basic fluid and calories until diuresis begins, and 50%-dextrose infusions *via* polythene cannulae into large veins are frequently used. However, the risk of thrombosis around the cannula is great,[9] and although embolization from this site is uncommon, it is probable that prolonged anticoagulant therapy would be beneficial in preventing the occurrence of thrombosis.

Haemodialysis for renal insufficiency does not increase the risk of thrombosis and subsequent embolization.

SUMMARY

1. The principle of the 'artificial kidney' and the constitution of a metabolic unit for the purpose of haemodialysis are described.

2. Three cases who underwent haemodialysis are reported. One was a case of chronic renal insufficiency and the other two were cases of acute renal insufficiency. Although these cases died ultimately, the beneficial effect of haemodialysis was apparent.

3. The ease of operation of the Travenol 'disposable twin-coil kidney' is stressed, and the methods used in countering the few practical difficulties that arose are described.

I wish to thank the Medical Superintendent of the Ernest Oppenheimer Hospital, Dr. T. Leontsinis, for helpful suggestions and criticism in the preparation of this paper, and am indebted to him and to the Medical Consultant of the Anglo American Corporation for permission to publish these cases. My thanks are also due to the medical staff and the laboratory technologists of the hospital for their cooperation and assistance.

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THE ELECTRICAL PULSE DUPLICATOR—ITS USE IN TESTING VALVE PROSTHESES WITH SPECIAL REFERENCE TO THE AORTIC AND MITRAL VALVES

C. N. BARNARD, M.D., M.MED. (CAPE TOWN), M.S., PH.D. (MINNESOTA); M. B. MCKENZIE, M.B., CH.B. (CAPE TOWN); and D. R. DE VILLIERS, M.SC., M.B., CH.B. (CAPE TOWN) *Department of Surgery, University of Cape Town*

Progress in modern open heart surgery and the use of cardioplegic drugs,[1-3] retrograde perfusion of the coronary sinus,[4] or other means of supporting the myocardium during cross-clamping of the ascending aorta, has made direct surgery on any of the four valves of the heart possible. At present there appears to be general agreement that the ideal correction of acquired valvular defects awaits the development of suitable prosthetic valves.

Before a prosthesis of any design can be used for the correction of a valvular defect in patients it should fulfil the following criteria:

(*a*) The prosthesis should be of such design that it can be inserted and secured in the limited space that exists in the annulus of the valve to be corrected.

(*b*) It should function freely under the conditions which exist at that particular point of the circulation and continue to function for many years.

(*c*) It should be tolerated within the circulation; that is to say, it should not be extruded as a foreign body.

(*d*) It should not damage the elements of the blood or the heart itself, or promote clotting of the blood with embolization.

Part of the work in testing fabricated prosthetic valves thus necessitates the study of valvular mechanics by dynamic demonstration of the action of these valves. If this is done under hydrodynamic conditions, similar to those present during life, such an investigation will determine whether the valve being tested will function freely and adequately when used for the correction of valvular insufficiency. By leaving the prosthetic valve to function under these conditions for long periods of time at speeds of 120-150 cycles per minute, fatigue can be studied, giving useful information on how the valve will withstand the systolic and diastolic forces throughout life.

The purpose of this paper is to describe a method by which prostheses for the correction of regurgitant aortic and mitral valves can be tested in a pulse duplicator to determine whether they fulfil some of the criteria listed above.

APPARATUS

The Electrical Pulse Duplicator

The important part of an apparatus used in testing prosthetic valves for the left side of the heart is a pulse duplicator capable of producing a pulsatile flow of fluid comparable in volume and pressure to the stroke of the left ventricle. An electrical pulse duplicator used by us for this purpose is illustrated in Fig. 1. This apparatus consists of a T-tube A, 1 inch in diameter. One limb of this tube is connected through a solenoid valve B, 1 inch in diameter, to a water tap. Water was found to be the most satisfactory

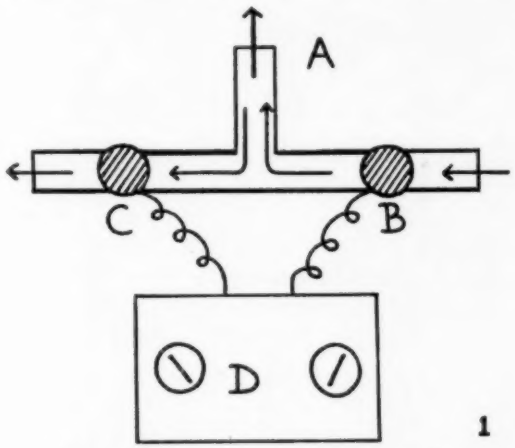

Fig. 1. Diagram of the electrical pulse-duplicator.

perfusion fluid for photographic purposes, and the water pressure in the tap provides inexpensive power for the pulsator. The second limb leads off to a drain through a second solenoid valve C, of similar diameter.

The two solenoid valves are electrically activated. The rate, and systole-diastole ratio corresponding to different rates, are controlled by two switches on control box D. This control system is constructed in such a manner that the one solenoid valve is open while the other is shut and *vice versa*. The third limb of the metal tube is connected to the testing chamber, which varies with each valve to be tested and the type of test done.

Testing Chambers for Aortic-valve Prostheses

In order to test an aortic-valve prosthesis, the duplicator is connected to two chambers, A and B, manufactured from quarter-inch-thick plexiglass (Fig. 2). These two chambers are separated by a disc C, in which the valve to be tested is inserted. It is possible to unscrew chamber A from chamber B, and also to unscrew the lid of chamber B, thus allowing insertion of the valve and operation on the valve once it is in position.

In order to observe whether the valve to be tested can be secured in the root of the aorta and whether it will function freely, the base of the aorta together with the aortic valve and half an inch of ventricular muscle and the aortic leaflet of the mitral valve are excised from a post-mortem human heart (preferably from a patient who died of aortic regurgitation) and attached between two strips of Ivalon as shown in Fig. 3A. When the purpose of the test is to see how long the prosthesis will last when subjected to forces similar

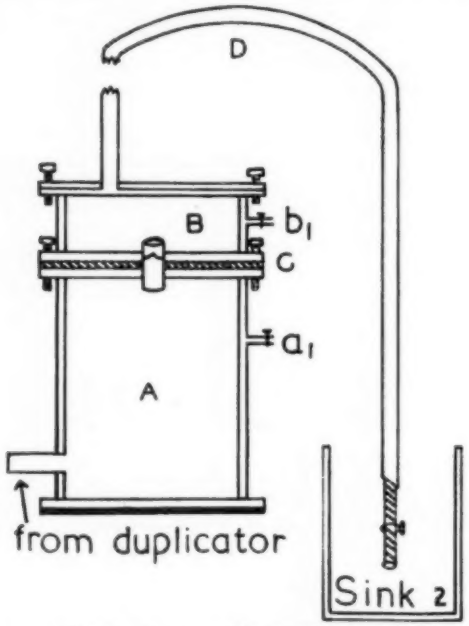

Fig. 2. Diagram of the testing chamber for studying the aortic valve.

to those in the circulation, it is set up as shown in Fig. 3B attached to a strip of Ivalon overlying an opening approximately the size and shape of the aortic valve in mid-cycle.

After the chambers have been screwed together with a valve in position the only connection between them is through the valve.

An inverted plastic U-tube D, 1 inch in diameter, is attached to the top chamber (Fig. 2). The length of the ascending limb of this tube can be adjusted so that, when filled with water, the desired pressure is exerted on the valve. The descending limb is connected by way of a compressible rubber tube to the water drain. The pressure in this tube can thus be adjusted further by partially clamping the rubber tube. This, in conjunction with the air trapped in the descending limb, will allow of elastic resistance simulating the peripheral resistance in the human circulation.

Testing Chambers for Mitral-valve Prostheses

When testing a mitral-valve prosthesis for strength and durability, the assembly is the same as for the aortic valve except that chamber A now has an outlet which leads to the drain (the aortic outflow) and chamber B, instead of the inverted U tube, has an adjustable water supply (pulmonary veins supplying left atrium)—Fig. 4A. The valve to be

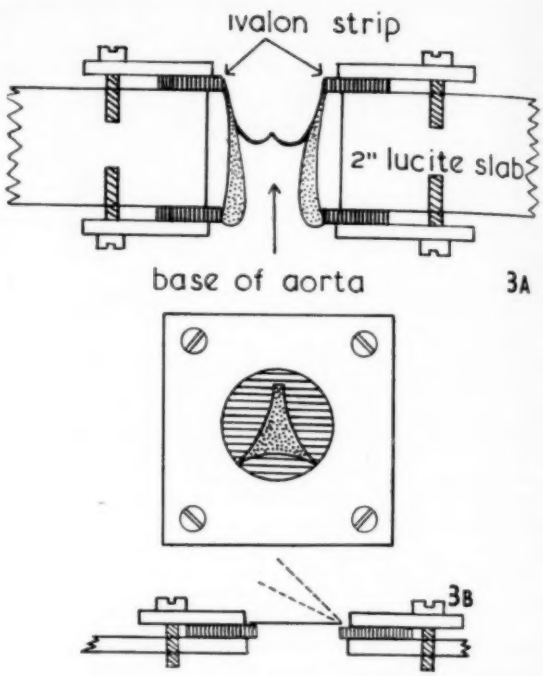

Fig. 3. Diagram showing the method of fixation of the aortic valve in the testing chamber: (A) For studying valve action. (B) For studying durability of the valve.

tested is secured in the manner described above in a piece of Ivalon. In order to see whether the prosthesis can be secured in the mitral annulus and whether it will function freely, the apparatus is set up as shown in Fig. 4B. A fresh human heart is removed at post-mortem (preferably from a patient who died of mitral regurgitation). The roof of the left auricle is excised below the entrance of the pulmonary veins. The left auricular appendage is ligated at its base and a linen purse-string suture is placed around the circum-

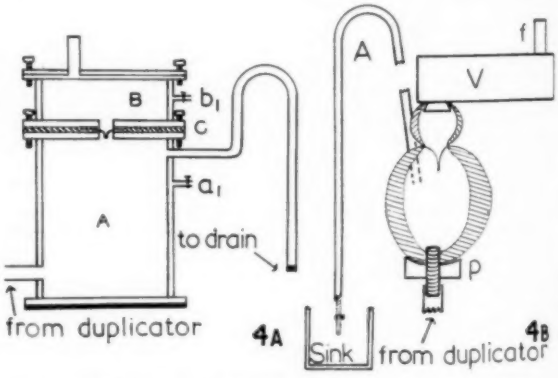

Fig. 4A. Diagram of testing chamber as used for the study of the durability of a mitral prosthesis.
Fig. 4B. Diagram showing the apparatus used for the study of the mitral valve.

ference of the auricular defect, through which the plexiglass viewing chamber V is attached. The roof of the aorta is dissected free from the pulmonary artery and the vessel is transected approximately 2 inches from its origin. A purse-string suture is placed about its circumference just proximal to the line of transection, to which the ascending limb of an inverted plastic U-tube A is attached.

The apex of the left ventricle is amputated so as to afford entry to the ventricular cavity and a thick linen purse-string suture is placed around this opening. A metal tube which passes through a cylindrical plexiglass block P is screwed through the hole in the apex into the left ventricular cavity and secured in position by tying the purse-string. The heart rests on the cup-shaped upper surface of the plexiglass block; the other end of the metal tube is connected to the duplicator. The heart and tubes attached are supported by suitable stands. The test can now be started. By unscrewing the lid of the viewing chamber V, the valve to be tested can be secured in the annulus of the heart.

METHOD OF TESTING VALVES

Aortic valve. The testing chambers and valve to be tested are set up as described above and connected to the pulse duplicator. Inlet valve B, is opened, the water tap turned on, and the system filled with water, expelling all the air. When this is complete the control box is switched on and the speed and systole-diastole ratio adjusted to give the desired rhythm of pulsation. The pressure changes in the two chambers (left ventricle and aorta) are measured by connecting taps a_1 and b_1 to a pressure-recording device. By adjusting the water inflow, the height of the ascending limb of the inverted U-tube, and the resistance in the descending limbs, the output per minute and pressure changes closely simulating those in the human circulation can be obtained (Fig. 5). The action of the valve can be observed and photographed through the top of chamber B (Fig. 6).

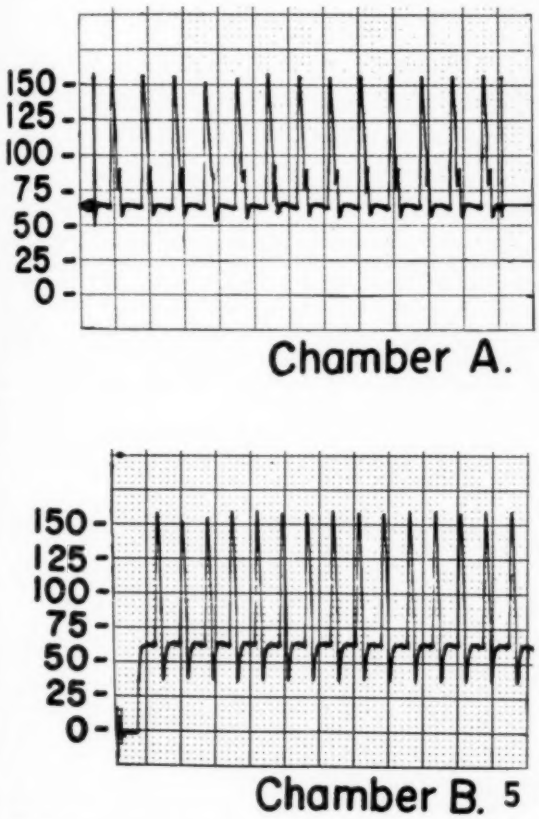

Fig. 5. Pressure tracings recorded while studying a competent aortic valve.

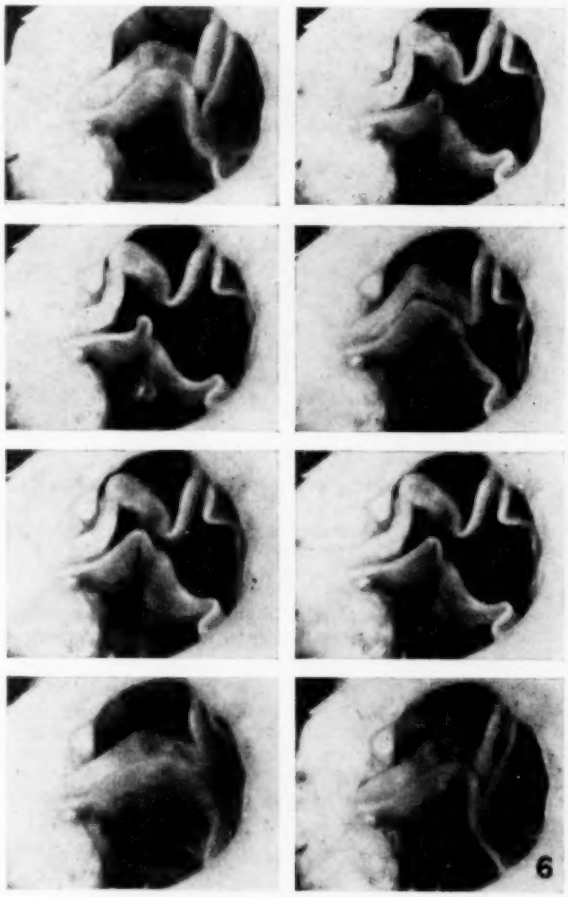

Fig. 6. Cycle of normal aortic-valve movements showing the opening and subsequent closure.

Mitral valve. The testing chambers are connected as described and connected to the pulse duplicator. The system is filled with water as for the aortic valve, systole and diastole adjusted, and pressures recorded in the top and bottom chambers (left auricle and left ventricle). The diastolic loss of fluid from the viewing chamber into the ventricles is compensated for, by the constant addition of water *via* the water supply f (Fig. 4B). It is essential to maintain the fluid level in this chamber during photography of the valve in

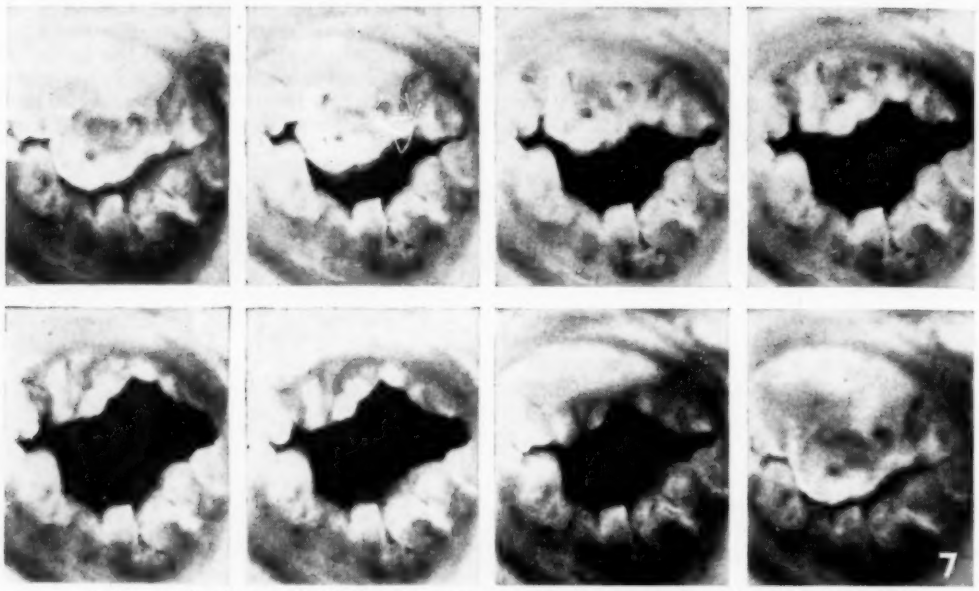

Fig. 7. Cycle of normal mitral-valve movements showing the opening and subsequent closure.

order to avoid the presence of bubbles or a receding water meniscus, which may impair visibility. The action of the valve can be carefully observed and photographed through the top chamber (Fig. 7).

CONCLUSION

The use of the artificial pulse duplicator makes it possible to study the action of normal and abnormal aortic and mitral valves under conditions of pressure and flow similar to those present in the beating heart. Intrinsic valvular action, however, cannot be evaluated in such a system, but despite these disadvantages the apparatus has proved to be of great value for the study of the action of prostheses designed to correct incompetent valves, and, in addition, such a system may be used to test the durability of a prosthesis under conditions similar to those found during life.

SUMMARY

The construction and method of operation of a simple inexpensive artificial pulse duplicator is described. Such a system enables one to study and photograph the action of normal and abnormal valves and also to study and test prosthetic valves under conditions of pressure and volume flow similar to those existing in the normal circulation.

We are most grateful to the United States Public Health Department, the South African Council for Scientific and Industrial Research, and the University of Cape Town Research Grants, for valuable financial assistance. We should also like to thank Mr. C. C. Goosen, technician to the Department of Surgery, University of Cape Town, for the photography of diagrams and figures included in this article, and Mr. J. Linney, representative of Messrs. A. Lalieu (Pty.) Ltd., for making a film of the opening and closing of the valve, from which we have taken Fig. 7.

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THE TUMBU FLY, *CORDYLOBIA ANTHROPOPHAGA* (BLANCHARD), IN SOUTHERN AFRICA*

F. ZUMPT, *Department of Entomology, South African Institute for Medical Research, Johannesburg*

Cordylobia anthropophaga, the 'Tumbu fly' or 'skin maggot fly' is widespread over the Ethiopian region, i.e. Africa south of the Sahara, but it does not occur in any other zoogeographical region of the world. In West and Central Africa it is a very common pest; the larvae affect mainly humans, dogs and various kinds of rats, but they are also occasionally found in other wild and domesticated mammals.

* Paper read at the National Meeting of the Dermatological Sub-group of the Venereology and Dermatology Group (M.A.S.A.), Pretoria, 28 March 1959.

In the Union of South Africa this parasite has become of greater importance only in recent times. Drs. Annie Porter and Heymann,[1] who submitted a paper on this fly at a meeting of the Medical Association in Johannesburg on 19 December 1929, 30 years ago, said that 'in the Union of South Africa such cases are relatively uncommon'. They presented a case of a 9-months-old European girl who had contracted the infection during a short stay in the Bulawayo district, S. Rhodesia.

De Meillon and Gear,[2] in 1947, said that the Tumbu

fly was already very well known in the subtropical regions of Southern Africa, such as the Transvaal Lowveld, Natal and Zululand, but that for the first time specimens from human patients had been sent to the South African Institute for Medical Research from the Transvaal Highveld. There had apparently been a minor epidemic at Witbank, and several locally contracted infections had been found in the environs of Johannesburg, Pretoria, Springs and Lichtenburg.

Since then, we have received many more records of human infections with *Cordylobia* from Southern Africa, and de Meillon and Gear's assumption that the Tumbu fly has continuously enlarged its territory has proved to be true. The distribution of cases is shown in the map in Fig. 1, and in Table I, which includes the reliable† records known to me from our own cards and from the literature. It will be seen that human infection with *Cordylobia anthropophaga* has occurred widely in the Transvaal and the neighbouring part of the Orange Free State. It must be noted that when larvae extracted from humans are sent to us, it is not always certain that the infection has really been contracted in the district where the patient lives, even when he maintains that this is so. The larvae may stay in the human for quite a long time, longer than in their normal hosts, the rats, and the patient may have contracted the infection on a trip to the Lowveld or some other subtropical part of Southern Africa (see below). But for the practitioner this fact is not of such great importance as for the epidemiologist. The practitioner has to diagnose and to treat the infection wherever it appears in humans, and he should be acquainted with the aetiology and pathology of the disease.

TABLE I. RECORDS OF *CORDYLOBIA ANTHROPOPHAGA* (BLANCHARD) FROM SOUTHERN AFRICA

Locality and Date	*Stage*	*Host*
Ondongua, S.W. Africa. VI, 1934	L	*Tatera joanae* (= *T. afra*)
Outjo, S.W. Africa. III, 1953	L	man
Epukiro, S.W. Africa. III, 1950	L M F	?
Okahandja, S.W. Africa. III, 1951	L	man
Omitara, S.W. Africa	L	*Thallomys nigricauda* (= *Rattus paedulcus*)
Ondekaremba, S.W. Africa	L	*Tatera schinzi* (= *T. afra*)
Seronga (Ngamiland), Bechuanaland. VII 1949	M F	?
Shamva, S. Rhodesia	L	man
Bulawayo, S. Rhodesia	L	man
Messina, Transvaal	L	man
Pietersburg, Transvaal. I, 1941	L	dog
Letaba, Transvaal. I, 1915. XII, 1916	L	man, dog
Thabazimbi, Transvaal. IV, 1957	F	?
Nylstroom, Transvaal. III, 1957	L	man
Lydenburg, Transvaal. III, 1957	L	man
Rustenburg, Transvaal. XII, 1958	L	man
Koster, Transvaal. III, 1953	L	man
Pretoria, Transvaal (incl. Onderstepoort). I, 1915. XII, 1916. XII, 1939. I, 1944. X, 1948. I, 1949.	L	man, dog, guinea-pig
Witbank, Transvaal	L	man
Lichtenburg, Transvaal	L	man
Environs of Johannesburg (incl. Sandown, Bryanston, Springs, Yokeskei River). XI, 1909. III, 1949. III, 1953.	L	man
Klerksdorp, Transvaal. I, 1959	L	man
Stegi, Swaziland. I, 1951	L	man
Hoopstad, Orange Free State. II, 1955	L	man
Viljoenskroon, Orange Free State. II, 1953	L	man
Vredefort, Orange Free State. II, 1958	L	man
Harrismith, Orange Free State	L	man
Lourenço Marques, Mozambique. XII 1908	L	man
Durban, Natal	L	man

† Not all records in the literature are, of course, reliable. The late Mr. Bedford (1927), for instance, wrote that he had taken numerous adult flies of *C. anthropophaga* 'at the entrances of wart-hog burrows' in the Northern Transvaal and in Zululand. He also said that the larvae parasitize wart-hogs and ant-bears. Bedford had confused *C. anthropophaga* with *Auchmeromyia bequaerti* Roubaud, which is very common in these areas and the larvae of which live as blood-suckers on wart-hogs and ant-bears. These two hosts, however, have never been found infected with larvae of the true Tumbu fly.

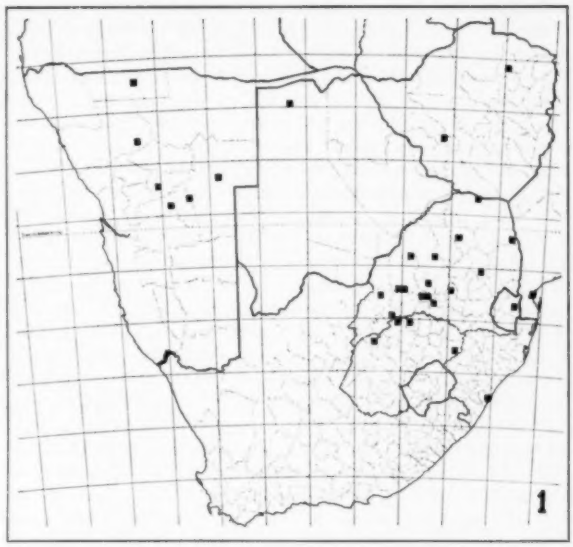

Fig. 1. Map of Southern Africa showing distribution of *Cordylobia anthropophaga.*

LIFE-HISTORY

The adult fly is rarely seen in nature, but it may be found in houses and huts, resting in dark places during the day-time. Males and females are very similar to each other, of yellow and dark-brown colouring, and measure 6–12 mm. in length. They become active in the late afternoon and in the early morning. At night they rest too, but may be attracted by artificial light.

The adult fly does not live parasitically, but feeds, like many other blowflies (fam.: Calliphoridae), on the juices of plants, for instance bananas, pine-apples and other fruits, and also on decomposing animal substances and on excreta. For oviposition, the female is especially attracted to dry sand which has been contaminated with urine or faeces. If the sand is still too moist, eggs are not laid there but are often deposited near by on a dry spot. Blacklock and Thompson[3] (1923), in their excellent study on *C. anthropophaga* in Sierra Leone, reported on an experiment in which wet sand had been provided for a mature female fly. She landed on it and protruded the ovipositor, 'but apparently found it too wet', flew off again and deposited about 100 eggs in a plug of pink cotton wool. This observation is important in respect of human cases, the flies being attracted to, and

stimulated for oviposition by, the soiled napkins of babies. They do not deposit their eggs on the wet clothes, but near by on the dry parts. If these napkins or other soiled clothes are not properly cleaned and ironed (they may appear quite clean to the human eye and nose), the flies may be attracted to them, for oviposition, in the same way as to dry contaminated sand. However, the flies will oviposit only in a shady place; if the clothes are hanging in the bright sunlight the flies will not deposit eggs, and any eggs that have been deposited previously or any young larvae will be killed immediately by the heat of the sun. I should add that the flies never deposit their eggs on the naked skin nor attach them to the hairs.

The stages in the life history are shown in Fig. 2. The female fly lives for only about a fortnight and during this time produces 300–500 eggs, which, as a rule, are deposited in two batches. The average length of the egg is 0·8 mm. At room temperature the larvae normally hatch on the 3rd day. They measure from 0·75 to 1 mm. The larvae remain in the situation in which they have hatched out, just below the surface of the sand, waiting for a host. If the surface of the sand is touched by any object, the larvae quickly crawl up. They adhere to grains of sand, by means of their posterior

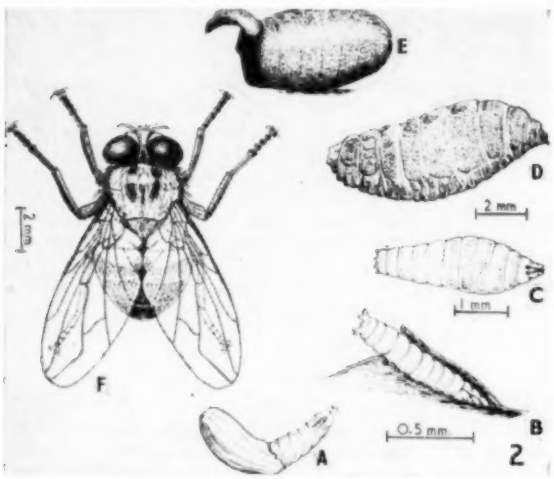

Fig. 2. Life cycle of the Tumbu fly, *Cordylobia anthropophaga* (Blanchard). A = larva hatching from egg. B = 1st larval stage. C = 2nd larval stage. D = 3rd larval stage. E = pupa. F = adult fly.

ends, raise their bodies into the air and wave about quite actively, seeking a host to which they can attach themselves. The same effect can be produced by bringing a container with hot water near the surface of the sand. The larvae remain alive in the sand for about 2 weeks; after this time they either die or become incapable of invading the host's skin.

Once a larva has succeeded in becoming attached to the skin, it immediately starts to penetrate. The time required for complete penetration depends on the thickness of the skin. On a rat or a guinea pig it takes from 25 seconds to about ½ hour. At the end of the process of invasion the larva is covered by a thin layer of skin; its last segment protrudes slightly from the aperture, but can be withdrawn when touched.

The 2nd larval stage arises as the result of a moult which occurs in the tissues of the host about the 3rd day after penetration. The larva then measures from 2·5 to 4 mm. and is quite different in shape. The 3rd and last moult, again in the tissues, takes place on the 5th or 6th day. The 3rd stage is again different from the 2nd, so that all three stages may easily be distinguished from one another. In a rat the larva reaches maturity about the 8th day, when it measures 13–15 mm. in length. Under normal conditions the larva then leaves its boil, drops to the ground, and pupates there within 24 hours. The puparium has a length of 6–12 mm. At room temperature the fly hatches after 10–11 days; at lower temperatures the pupal stage lasts longer.

Blacklock and Thompson found that in Sierra Leone the wet season is the season of prevalence of infections with *Cordylobia* larvae. The same is true for Southern Africa, as can be seen from Table I.

BEHAVIOUR IN MAN

Although the first larval stage of *Cordylobia anthropophaga* penetrates the skin of many mammals and even of birds, it does not follow that after establishment in the host-tissues development to maturity will take place. This is a matter of great significance and throws light on the question whether we are dealing with a suitable host or not. From this point of view, man must be listed as one of the unsuitable (or at least less suitable) hosts; he is, nevertheless, commonly attacked.

Blacklock and Thompson undertook some experiments with human volunteers. A larva measuring 0·9 mm. in length was placed on the back of a finger of an adult European. The larva moved quickly into a wrinkle and started to penetrate at once. No sensation was felt. Ten minutes later the larva was half concealed and first itching was felt. After another 10 minutes the larva was completely concealed in a tunnel. After 2 hours the itching became constant and a redness and swelling were visible around the larva. The next day a definite papula had been formed, but the irritation had ceased. By the second day the papula had grown larger, but no itching or other irritations were felt. Thereafter, the papula gradually disappeared without any itching or other discomfort. This experiment was repeated several times with other Europeans, and also with two Africans, with similar results. The French authors Roubaud and Bouet had previously had similar experiences in Senegal.

In all these cases the Europeans and Africans had a natural resistance or an acquired immunity (see below) which prevented further development of the larvae. There are several kinds of animals which react in the same way. But there are many cases, as we know from our own experiences in South Africa, in which the larvae succeed in continuing their development in the human skin. Blacklock and Thompson followed up the further development in several Europeans. As in the above-mentioned experiments, it was found that the larvae caused a slight itching or pricking at intervals in the first 2 days, symptoms which may easily be overlooked. The papulae continued to increase in size and became red, but the irritation ceased more or less completely for several days. Then the symptoms suddenly recurred with much greater severity, the pain increased and in some cases became so sharp as to interfere with sleep. At intervals the larvae became very active and could be seen retracting into the cavities and then pushing against the margins of the aperture

in order to increase their size. Serous fluid was exuded, the tissues had become indurated and the area around the aperture was deeply coloured. A tenderness existed on pressure. The lesion then resembled a boil. Even glandular enlargement was found to occur, as well as general symptoms like malaise and febrile reactions.

The development then became slow in the human volunteers, and in one case a 3rd-stage larva removed on the 15th day was found to measure only 9 mm. in length. In rats and guinea-pigs the larvae normally reach maturity on the 8th day, when they measure 13–15 mm.

In humans the larvae are usually noticed only when the 2nd or, more commonly, the early 3rd stage has been reached. The larva is then enlarging its aperture with considerable force and probably produces a lytic reaction on the tissues. A clear fluid comes from the cavity at intervals, sometimes stained with blood or with the faeces of the larva.

Nagel (1897) recorded that in East Africa he observed a larva in his skin for a period of 4 weeks. Evidently this larva also failed to complete its development.

These observations speak for the theory that man is an unsuitable host for *Cordylobia anthropophaga*, in that the parasite is not able to complete its development in man's skin. The larvae which I have received from humans have never been fully mature, but have at most reached the early 3rd stage. Of course, no patient would allow the larvae to continue their development after he had felt the first real pain or after the boil had reached an alarming size. Blacklock and Thompson followed up the infections of only a few volunteers, and it may be possible that there are humans in whom larvae may really reach maturity. I doubt it, and it will probably never happen in nature, but unless this is disproved on more volunteers from different areas and of different races the probability cannot be completely excluded, and man cannot be definitely listed as an unsuitable host for *C. anthropophaga*.

ACQUIRED IMMUNITY IN MAN AND ANIMALS

As the above-quoted experiments have shown, many of the larvae of *C. anthropophaga* do not continue their development in the human skin beyond the 2nd day. This phenomenon can be explained on the basis either of a natural resistance or of an acquired immunity resulting from a previous infection.

Blacklock and Thompson, to some extent, dealt with this problem, too, and recorded the case of an adult European in Sierra Leone who had suffered from a natural infection in which 9 larvae developed in the skin, reaching a length of 6–8 mm. when they were removed. Thereafter he proved resistant to experimental infection at several attempts 4–7 months afterwards, the larvae dying on each occasion.

Similar results have been obtained with dogs, monkeys and guinea-pigs which had previously been infected with positive results. This acquired immunity, however, does not seem to last very long. A European who had contracted an infection in the Congo went back to Europe. Just over a year later he returned to the Congo and promptly became infected a second time. Exactly the same thing happened to his dog.

Blacklock and Thompson have also obtained some paradoxical results. A Coloured youth had received an infection of 4 larvae on 7 March 1923, which developed to papules only; on 8 April he contracted another infection by a single larva, which developed to the 3rd stage. A similar result was obtained with a small dog.

Unfortunately, Blacklock and Thompson did not undertake immunity experiments with rats, the main hosts of *Cordylobia anthropophaga* in nature. In the field, adult rats are often found infected with a great number of larvae, which may cause the death of the host. It may be that those rats did not have a previous infection, or that the immunity broke down later owing to some unknown cause. These are the conclusions drawn by Blacklock and Thompson. It may also be possible that the rats are not able to build up an immunity at all.

TREATMENT

The larvae may be expressed by digital pressure. It is advisable to cover the lesion with petroleum jelly some time before. The larva, which is now excluded from air, will make strenuous efforts towards the aperture, thus facilitating extraction. After extraction, the wound heals easily, but a mark remains for a long time.

The larvae of the 2nd and 3rd stages are not able to invade the skin again, so that they are quite harmless after extraction. They should be preserved in 70% spirit (under no circumstances in formalin) and sent to the Institute with a full case history, so as to add to our knowledge of this parasite and its medical significance. We are also very interested in seeing patients with advanced and heavy infections in order to get some new photographs.

I wish to thank all the doctors who have provided us with material and case histories of *Cordylobia* infections. Furthermore, I am indebted to Mr. D. H. S. Davis, Head of the Medical Ecology Centre, for the map prepared in his department.

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WORLD HEALTH ORGANIZATION

WHO REGIONAL COMMITTEE FOR AFRICA *

The report which I have the honour to place before the Committee this year, and which deals with the period 1 July 1958 to 30 June 1959, is intended to reflect the present health situation in the African Region. This gives me the opportunity to say that the situation itself gives me cause for sober satisfaction in some respects, but for continued concern in others. There are indeed some sectors in our far-flung battle line against disease where the enemy is in full retreat. The massive campaign against yaws, which has already reached 17 million people examined, of whom more than 8 million have received the required treatment, has brought eradication within sight: notably in Liberia and Nigeria.

A most encouraging development has taken place in Nigeria. As the mass campaign against yaws reached the integration stage, a spontaneous movement among the population of certain regions resulted in the raising of voluntary contributions to develop and maintain rural health centres to deal not only with the remnant

*Abstract of Address to 9th Session by Dr. F. J. C. Cambournac, Director, African Region, WHO.

of the yaws problem but also to watch over the general well-being of the people. Here is a wellnigh perfect instance of one of the fundamental principles of WHO, as defined in our Constitution, in process of application: 'Informed opinion and active co-operation on the part of the public are of the utmost importance in the improvement of the health of the people'.

Equally encouraging is the increase in rural health centres established by public health authorities in a number of countries. With the dispensaries under their control, they are not only of direct benefit to the people, they also serve as a useful training ground for medical personnel, particularly auxiliary personnel; while they may be of the utmost value in the final phase of surveillance in control campaigns against specific diseases.

Where leprosy is concerned, more than 1 million of the estimated total of 2,300,000 cases in Africa are now under treatment with sulfones and it is expected that nearly *all* will be reached in the future. In fact, at the present rate of progress, it is not too much to hope that the present generation will be the last to undergo this terrible affliction, as was emphasized at the Conference on Leprosy in Africa held in Brazzaville last April under the joint auspices of the Regional Office for Africa of the WHO and the Commission for Technical Cooperation in Africa South of the Sahara.

A considerable expansion has taken place in antituberculosis work. Nearly every country in the African Region has asked for the services of the two WHO Tuberculosis Survey Teams, to which a third is being added. Another interesting development is the establishment of a centre for the analysis and coordination of tuberculosis work in Africa, which will shortly be functioning here in Nairobi. In this way, the necessary epidemiological information will be gathered for control campaigns. In addition, several mass chemo-prophylaxis projects are already under way or being planned in various territories of the Region, including Kenya and Mauritius.

Where smallpox is concerned, the control campaigns carried out by governments have resulted in the reduction of this disease to very small proportions, while eradication has been achieved in certain areas. We have requests from several governments for WHO services to organize smallpox eradication campaigns on a large scale.

However, there are other sectors where we are encountering difficulties, both strategic and tactical. In attempting to apply the global malaria eradication programme of WHO in the African Region, we are faced with complications, absent elsewhere, which have given us pause and forced us to reconsider and improve our methods, through survey and research, before redeployment of our forces. True, in certain areas, including the Southern Cameroons, the southern part of the Federation of Rhodesia and Nyasaland, Kenya, Swaziland, the Union of South Africa, and Mauritius, the by now classical, method of spraying with residual insecticides has interrupted transmission and the surveillance stage has been reached. Also, the coordinated inter-country eradication campaign, planned and concerted at a meeting of technical experts at Lourenço Marques last year, among a number of countries of south-east Africa, which is intended to reach more than 4 million people, promises well, particularly because research and previous control campaigns conducted by the governments themselves have shown excellent results, and also because much of the money needed for the joint eradication campaign has already been allocated.

But, in other parts of Africa, we are continuing the search for the right combination of methods to achieve eradication because, in many instances, local epidemiological conditions complicate the issue. Nevertheless, it can be said that the results of surveys and research so far obtained give a hopeful indication that, in the near future, malaria eradication will be feasible and become an accomplished fact throughout Africa. Of course, there are still other diseases whose control raises difficult problems, among which I will mention only one, bilharzia.

Although great efforts have been made by public health authorities in many countries to deal with other health problems which are of importance to all of us, such as maternal and child health, environmental sanitation, nutrition, provision of nursing services, and mental health, much remains to be done. It is both the duty and the desire of the WHO to assist governments in these fields to the utmost of its capacity. But we have to recognize that we have a very long way to go before we can claim that health conditions anywhere in Africa can compare favourably with those areas where standards are high and where communicable diseases generally have ceased to be important public health problems. And, furthermore, our task is made at once more difficult and more vitally important by the tremendous economic development which is now taking place in most parts of this vast continent. We must be ever on the alert lest economic expansion produce fresh health hazards; in fact, we should insist that health considerations are adequately recognized at the earliest planning stages of all economic development.

It is in this context that the subject chosen by the Regional Committee for our technical discussions: 'Medical aspects of urbanization in countries South of the Sahara', gains added significance, of all forms of economic expansion it is precisely urban development which contains the greatest potential health risks. Nor should the social aspects be overlooked. The rapid formation of large aggregations of urban and industrial populations creates problems over and above those of housing, sanitation and the provision of health services; particularly when such populations undergo a sudden transformation from tribal to urban and industrial patterns of society. Fortunately, we now have at our command a body of knowledge contained in the medical and social sciences which, it is hoped, will enable us adequately to guide this development.

It is in this connection, also, that our relations with other international organizations are so important. We have continued our close cooperation with the United Nations Children's Fund which participates, by means of providing supplies and equipment, in most of the WHO projects in operation or planned in the Region. Where the health aspects of nutrition are concerned we remain in close contact with the Food and Agriculture Organization of the United Nations. In addition, we continue to work together with the Commission for Technical Cooperation in Africa South of the Sahara and its Scientific Council. An important recent development has been the establishment of the Economic Commission for Africa by the United Nations itself, as well as the United Nations Special Fund whose policy is, among other things, to initiate projects to demonstrate the wealth-producing potential of unsurveyed natural resources. In view of what I have already said, it will be clear that great importance should be attached to the closest possible working relationships between those bodies and our Regional Organization, particularly as regards the health aspects of economic and social development.

The same applies to the International Cooperation Administration of the United States of America, with whom we also co-operate closely, particularly in Liberia.

In closing, I should like to express my appreciation to the Government of Kenya and the City Council of Nairobi, whose officials have done so much, in their quality as our hosts, to help prepare for our present session which, I am certain, will prove constructive and fruitful in its deliberations.

PASSING EVENTS : IN DIE VERBYGAAN

New X-ray System. Medical X-ray images were transmitted over closed-circuit television from the chest clinic of Cook County Hospital, USA, to a scientific exhibit at the Palmer House, Chicago, USA, where they were viewed by medical educators from more than 60 different countries who were attending the Second World Conference on Medical Education. The medical X-ray system, called TVX, was used by physicians of the Northwestern University Medical School to demonstrate results of research made possible by this unique X-ray viewing method developed by the X-ray department of the General Electric Company. The Northwestern doctors transmitted the X-ray images, which under standard conditions would be seen only on the fluoroscopic screen of the X-ray table at the actual site of the examination. The transmission was by microwave for a closed-circuit system and presented to the convention delegates on 10 television screens at the Palmer House.

Alternating with the X-ray image was a standard closed-circuit viewing of the actual X-ray room scene at the hospital enabling delegates at the Palmer House to receive a complete picture of the examination taking place. Comments of the examining radio-

logist at the hospital were transmitted over a two-way audio circuit with the demonstrating physician at the exhibit. This TVX transmission is unlike conventional closed-circuit television presentations or previous X-ray intensifying methods in that it does not involve photography. The examining radiologist views the X-ray image on the TVX screen—just as the remote observer does. The advantages are many. Diagnosis can be made under normal TV lighting conditions, rather than in a completely darkened room, as is necessary with standard fluoroscopy. Also, the TVX image can be transmitted to one or more remote viewing areas. This X-ray progress is due to the development by General Electric of an X-ray sensitive camera tube which allows direct transfer of X-ray energy to electron energy capable of being displayed on a television screen. The TVX system is used in conjunction with conventional X-ray generating equipment, and is being made available for research purposes.

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Dr. Noel H. Aldridge, M.B., Ch.B., D.M.R.D. (R.C.P. & S.), L.M.C.C., Cert. Rad. (R.C.P. & S.), formerly Associate Radiologist at the Johns Hopkins Hospital, Baltimore, USA, and the Victoria Hospital, London, has now been appointed Director of the Department of Radiology, St. Joseph's Hospital, Sarnia, Ontario, Canada, and Consultant Radiologist to the Carruthers Clinic in Sarnia.

* * *

Paediatric Prize Essay, 1959. The South African Paediatric Association (M.A.S.A.) has awarded the Paediatric Prize to Mr. A. B. Ockerse, a 6th-year student at the University of Pretoria, for the second year in succession. The title of the essay was 'The aetiology of gastro-enteritis in infants'.

The Paediatric Nursing Prize, which is awarded to the candidate obtaining the highest marks in the annual examination for the Certificate of Paediatric Nursing of the South African Nursing Council, was won by Staff Nurse A. M. S. Dicey.

The subject of the essay for the 1960 Prize has not yet been decided upon. The prize is an award of £10 and a bronze medal if the essay is of sufficient merit.

* * *

Dr. Joseph Wolpe, M.D., part-time lecturer in the Department of Psychiatry at the University of the Witwatersrand, has been appointed to the post of Research Professor in the Department of Psychiatry, University of Virginia, Charlottesville, Virginia, USA. Dr. Wolpe will take up his appointment in January 1960.

* * *

Enteric Fever. While the general standard of health of Natives employed on mines of the Anglo American Corporation Group had shown little change over the past 5 years, enteric fever, which had been practically non-existent for many years, is gradually making its re-appearance in gold mines and collieries. This 'disturbing factor' is disclosed in the 1958 report of Dr. J. H. G. van Blommestein, Medical Consultant to the Anglo American Corporation of South Africa, Ltd. The disease is manifesting itself again, he states, notwithstanding the fact that all new recruits to the mines receive a full prophylactic vaccine course. 'One is reluctantly forced to the conclusion', the report adds, 'that the vaccine is not affording the protection which it gave in the past'. The report discloses that respiratory diseases, including pneumonias, influenzas and bronchitis still take the greatest toll in sickness among the Native employees. The incidence of both forms of pneumonia appeared more or less unchanged in the older gold mines but in the Orange Free State there had been an overall increase in the rates. One of the many factors influencing this rate, says the report, was that the Orange Free State mines had a much greater percentage of labour drawn from tropical areas.

* * *

Lede word daaraan herinner dat hulle die Sekretaris van die Mediese Vereniging van Suid-Afrika, Posbus 643, Kaapstad, sowel as die Registrateur van die Suid-Afrikaanse Geneeskundige en Tandheelkundige Raad, Posbus 205, Pretoria, moet verwittig van enige adresverandering. Versuim hiervan beteken dat die *Tydskrif* nie afgelewer kan word nie. Dit het betrekking op lede wat oorsee gaan sowel as dié wat binne die Unie van adres verander.

* * *

South African National Tuberculosis Association, Case-finding. Some years ago the discovery of TB cases through the medium of X-ray examinations presented those concerned with the control of tuberculosis in South Africa with a serious problem. With the TB incidence conservatively estimated at 1% of the total population, i.e. approximately 130,000 cases, and a serious shortage of TB beds in which to treat them, medical men had their hands full dealing with notified cases and were not anxious to go out seeking new cases when treatment facilities were so inadequate. Within the last 5 years, however, the position has vastly changed. The number of TB beds in the country has been increased to 20,000 from all sources—government, local authority, SANTA, mission and private hospitals. In addition, with modern drugs it is possible to treat many hundreds of early cases at home. Therefore in the overall control of tuberculosis, case-finding is assuming more prominence, and ways and means of ensuring that case-finding programmes will become even more effective were discussed by SANTA at its National Meetings in East London last month. The central Government (which has a number of mobile mass miniature radiography units in operation throughout the country) and local authorities (many of which have their own stationary units and receive a proportionate refund of their expenditure in this connection from the Department of Health) are responsible for the provision of X-ray facilities, but SANTA will press for the Department to provide increased financial assistance to all municipalities so that group surveys may be undertaken throughout the country. In this way a clear picture of the actual incidence of tuberculosis in South Africa can be established and plans for control made accordingly.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

LARGACTIL

Maybaker (S.A.) (Pty.) Ltd. announce the introduction of Largactil 50 mg. tablets in packs of 50 and 500. It is considered that there is a demand for a Largactil tablet of this strength which will minimize the number of tablets required to treat patients on a dosage of under 100 mg. In addition, 50 mg. tablets will help to ensure that adequate dosage of chlorpromazine is given when dosages higher than 25 mg. have been prescribed.

The range of Largactil preparations now includes tablets of 10 mg., 25 mg., 50 mg. and 100 mg.; syrup containing 25 mg. chlorpromazine hydrochloride in each fluid drachm; 1% injection in 5 c.c. ampoules; 2·5% injection in 1 c.c. and 2 c.c. ampoules; and suppositories of 100 mg. chlorpromazine base.

ENDOXAN

Noristan Laboratories (Pty.) Ltd. introduce Endoxan (N, N-Bis(B-chlorethyl)-N′,O-propylene-phosphoric ester diamide) and supply the following information:

Endoxan is a cytostatic agent for the treatment of tumours, leukaemia, lymphogranulomatosis, etc. It is of especial value for protective therapy, i.e. following surgery or radiation treatment and to prevent post-operative relapse.

It is well tolerated and side-effects such as nausea, vomiting or headaches occur only rarely, after high doses. In a few isolated cases it may cause temporary loss of hair.

Indications. Protective therapy to prevent relapse after surgery or radiation treatment; tumours with disseminated growth; chronic lymphoid and myeloid leukaemias; and lymphogranulomatosis, lymphosarcoma and other types of reticulosis.

Administration and dosage. Treatment usually commences with intravenous injections, but the intramuscular route may be used if preferred. It is also possible to give intrapleural, intraperitoneal or intratumoural injections of this preparation.

Endoxan is supplied in vials with an admixture of sodium chloride. 100 mg. is dissolved in 5 ml., or 200 mg. in 10 ml. *Aq. dest.* Inject the solution into the vial and shake for half a minute. Allow to stand until the solution is quite clear. Use immediately, or within 2-3 hours at the latest.

Dosage is determined in accordance with the patient's needs, taking into account his reaction and blood picture. If the first intravenous injection of 100 mg. is well tolerated, the dose is

increased to 200 mg. per day until a total of 4,000 - 8,000 mg. has been injected. If the white-cell count shows a tendency to fall, it may be advisable to inject not more than 200 mg. every 2-3 days. The treatment must be discontinued if the white-cell count falls to about 50% of normal. Cases of high-grade leukopenia may require blood transfusion and administration of ACTH or cortisone.

For continuation therapy tablets are recommended, in a dose of 100 - 200 mg., although this may be increased. It is essential to check the patient's general condition, blood picture and clinical findings regularly.

Endoxan is supplied in packings of 10 and 50 vials of 100 mg. Endoxan with 45 mg. NaCl; 10 and 50 vials of 200 mg. Endoxan with 90 mg. NaCl; and 50, 200 and 500 tablets of 50 mg.

Endoxan is manufactured by Asta-Werke AG, Brackwede, and the sole South African distributors are Noristan Laboratories (Pty.) Ltd., Silverton, Pretoria.

BOOK REVIEWS : BOEKBESPREKINGS

MUIR'S PATHOLOGY

Muir's Text-book of Pathology. 7th edition. Revised by D. F. Cappell, C.B.E., M.D., F.R.F.P.S., M.R.C.P., F.R.S.Ed. Pp. xx + 1,201. 733 figures. 70s. net. London: Edward Arnold (Publishers) Ltd. 1958.

The presentation of the 7th edition of this book differs little from the previous edition, thus retaining its familiar identity, but there are many additions and improvements, especially in the chapters on tumours. Benign and malignant tumours of specific tissues are now discussed together as they should be. Some of the less common tumours are included, such as alveolar soft-part sarcoma, histiocytoma cutis, molluscum sebaceum and chemodectoma, to name but a few. The aetiology of tumours has virtually been rewritten and includes many new facts on carcinogenesis and the effects of radiation and viruses on neoplasm.

There are considerable additions in the chapters on the haemolytic anaemias, the haemorrhagic diseases, renal tubular diseases and the endocrine disorders, because of the extensive advances that have occurred within recent years. The additions include accounts of auto-immunization, collagen diseases and supersensitivity; the effect of chemotherapy on the appearances of tuberculosis; Marfan's syndrome and endocardial fibro-elastosis; interstitial plasma-cell pneumonia; pulmonary siderosis, byssinosis and bagassosis; Xmas disease, afibrinoginaemia, hereditary telangiectasia and dysproteinaemia purpura; the tubular lesions of potassium deficiency; idiopathic hypercalcaemia with nephrocalcinosis, hyperphosphatasia and fibrous dysplasia of bone; and Klinefelter's syndrome.

Perhaps the most striking changes are to be noted in the illustrations. More than 100 completely new illustrations have been added to support the changes in the text, and in addition more than 40 illustrations have been substituted by improved photomicrographs of the same lesion.

These additions and alterations have been effected by adding only 111 new pages to the edition and increasing the overseas price from 62s. to 70s.

The value of past editions must be attributed largely to the unique approach to pathology of the author, the late Sir Robert Muir. And Prof. D. F. Cappell is to be congratulated on his revision, which has produced a book up-to-date in every way yet retaining so much of its original character. The reviewer regards this book as a fitting tribute to an outstanding pathologist of the old school and recommends it to the undergraduate as a remarkable text-book on general pathology. C.J.U.

CEREBRAL PALSY

Recent Advances in Cerebral Palsy. Edited by R. S. Illingworth, M.D., F.R.C.P., D.P.H., D.C.H. Pp. x + 389. 136 illustrations. 50s. net. London: J. & A. Churchill Ltd. 1958.

Recent Advances in Cerebral Palsy is essentially the product of the English school, although four of the fourteen contributors are from the USA. Prof. R. S. Illingworth has assembled a group of experts to contribute to a symposium which gives a picture of the present-day attitude to this condition. The contributors are all individuals who have had a great deal of experience in the handling of cerebral palsy in its numerous facets. The resulting book is one of the best balanced on the subject that have yet been published.

Professor Illingworth himself deals with the classification, incidence and causation as well as the early diagnosis of the handicaps of the cerebral palsied child. A well-known authority on the normal child, Professor Illingworth is exceptionally well equipped to deal with the handicapped child, and his clinic at Sheffield attracts handicapped children from far and wide.

Famous American experts who were active in the field of cerebral palsy long before the first clinic was started in the UK, are responsible for the chapters on 'structural changes in the brain' (Cyril B. Courville), 'recent advances in neurosurgery' (Russell Meyers), 'drug therapy' (M. A. Perlstein), and 'the role of physical therapy' (Winthrop M. Phelps). Prof. A. W. G. Ewing, of Manchester, writes on 'hearing disabilities', Norah Gibbs, of London, on 'psychological aspects', Ina Noton and Susanne Vincent, of Sheffield, on 'speech therapy', and F. Eleanor Schonell, now of Australia but previously of Birmingham, England, deals with 'intelligence testing'. G. A. Pollock, of Edinburgh, who read a paper at the S.A. Medical Congress in Pretoria in 1955, and W. J. W. Sharrard, of Sheffield, deal with the most controversial aspects of treatment 'the position of orthopaedic surgery'—a more balanced statement it would be hard to find. Alexander Innes, of Birmingham, describes equipment for home, school, and clinics. H. M. Cohen, Principal School Medical Officer, Birmingham, gives a review of the 'statutory and voluntary services' available in Britain. In Dr. Cohen's area every single cerebral palsied child is registered and is receiving treatment and care.

This book is one of the most important contributions to the knowledge and understanding of cerebral palsy. It is sane and well-balanced and will reward careful study. B.E.

CHOOSING THE SEX OF THE BABY

Son or Daughter by Choice. A guide to sex predetermination in humans and animals. By August J. von Borosini, Sc.D. Pp. 120. Illustrations. 23s. 9d. Amsterdam: E. J. Steinmetz. 1958.

This is quite an absorbing little book, which claims a high probability of success in begetting boys or girls as desired if Dr. von Borosini's instructions are carried out.

The chapters on popular belief, customs and superstitions as well as scientific views of the past make very interesting reading. From these some pertinent facts have been collected by the author in his research, which he has very cleverly dovetailed with anatomical and physiological knowledge on the subject to evolve his plan. Timing of intercourse, position, vaginal acidity or artificially-produced alkalinity, the necessity for female orgasm should a boy be desired, and the converse, are amongst the factors involved. J.P.R.

HORMONE- EN MENSTRUASIE-STOORNISSE

Die Hormonale Behandlung von Zyklusstörungen. Ein Leitfaden für die Praxis. Von Dr. Med. Rolf Kaiser. viii + 48 Seiten. 38 Abbildungen und ein Anhang mit 10 Tabellen. DM 5.80. Stuttgart: Georg Thieme Verlag. 1958.

Hierdie klein boekie bevat nie veel wat nuut is nie, en is meer 'n kort handleiding by die gebruik van hormone in gevalle van menstruasiestoornisse. Die verskillende reeds bekende hormonale behandelinge in gebruik by menstruasie-afwykings word kort en duidelik saamgevat. Daarby word gebruik gemaak van duidelike skematiese illustrasies wat die verskillende skemas van behandeling met een oogopslag verstaanbaar maak.

Die boekie is dus van enige waarde vir die besige algemene praktisyn maar voldoen nie aan die vereistes van die student nie en as sodanig verdien dit dan 'n beperkte aanbeveling.

D.A.H.duT.